Background and Aims:: Inherited cerebellar ataxia is a rare disabling disease that lead to early death. Here we describe clinical characteristics of a large Malagasy family with this disease, share our experience of its screening, our difficulties in assessing transmission pattern.

Methods:: It is a prospective study, in Analamanga region from 2011 to 2020. We did consultation and follow-up of index cases in our department, did home visit of other family members. Those who completed direct interview and clinical examination, with obtained informed consent, were included. They underwent interview with standardized questionnaires, clinical assessment, and brain CT scan. A family tree was built. Penetrance, clinical characteristics, inheritance pattern were analyzed.

Results:: From 5 generations, 148 persons were identified, 57 of them were studied (32 alive and 25 dead), with 18 patients with cerebellar ataxia. Cerebellar ataxia was present in each generation, in both sex, with an autosomal dominant pattern. Age of onset of ataxia were between 30 and 50 years old for the first 3 generations and between 7 and 28 years old for the fourth generation. From the first 3 generations 15 dead at their third or fourth decade. Non-cerebellar neurological signs were dominated by early onset of cognitive disorders (n=21). Nowadays all those who had cerebellar ataxia are dead so we are waiting for their descendence to present its signs.

Conclusions:: Cerebellar ataxia with probably dominant autosomal inheritance pattern was observed. International collaborations are needed when studying this disease in low income countries.
ANTI-YO ANTIBODY MEDIATED PARANEOPLASTIC CEREBELLAR DEGENERATION WITH BREAST CARCINOMA: RARE CASE REPORT

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Background and Aims:: Paraneoplastic cerebellar degeneration is a rare, severely debilitating neurodegenerative syndrome with antibodies targeting Purkinje cells of the cerebellum. It has been associated with fever than 1% of cancers, including small cell carcinoma of the lung, breast cancer, Hodgkin lymphoma and gynaecologic malignancies. Anti-Yo antibody frequently associated with this syndrome and associated with poor prognosis. We are reporting a rare case report of anti-Yo antibody mediated cerebellar degeneration in patient with highly aggressive carcinoma of breast.

Methods:: A 48-year-old female presented with 6-month history of imbalance while walking followed by tremulousness of both upper limb and change in speech. There was no history of preceding systemic symptoms, drugs, hypothyroidism, stroke or encephalitis. Family history was negative. On examination she had small lump in right breast and palpable axillary lymph node. Neurological examination showed severe cerebellar ataxia, intentional tremor, scanning speech and titubation, suggestive of pancerebellar involvement. Rest of examination was unremarkable.

Results:: On evaluation, MRI brain showed moderate cerebellar atrophy. Paraneoplastic panel showed strongly positive anti-Yo antibody. Histopathology showed high grade carcinoma with medullary feature. Treated with surgery (MRM) followed by chemotherapy (adriamycin + cyclophosphamide), Steroid, PLEX, IVIG (2gm/kg). No clinical improvement was noted in patient at 6 months follow up.

Conclusions:: This case highlights that anti-Yo antibody mediated paraneoplastic cerebellar degeneration may present before their cancer diagnosis and associated with very poor prognosis. Early recognition followed by rapid initiation of treatment may be helpful.
HUMAN ALLOGENEIC BONE MARROW-DERIVED MESENCHYMAL STEM CELL THERAPY FOR CEREBELLAR ATAXIA: A CASE REPORT

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Background and Aims:: To date, there is no curable treatment option for non-hereditary degenerative cerebellar ataxia. Here we report the case of a patient with sporadic adult-onset ataxia (SAOA) who underwent allogeneic bone marrow-derived mesenchymal stem cell (MSC) therapy via the intrathecal route.

Methods:: A 60-year-old male patient visited our clinic complaining of progressive gait disturbance that commenced two years ago. Upon neurologic examination, the patient exhibited limb dysmetria and gait ataxia. Brain magnetic resonance imaging (MRI) revealed cerebellar atrophy whereas the autonomic function test was normal. The patient was diagnosed with SAOA. The medications that were initially prescribed had no significant effects on the course of this disease and the symptoms deteriorated progressively.

Results:: At the age of 64, the patient was treated with allogeneic bone marrow-derived MSC therapy. The subsequent K-SARA (Korean version of the Scale for the Assessment and Rating of Ataxia) scores demonstrated a distinct improvement up until 10 months post-administration. No adverse events were reported.

Conclusions:: The improved post-treatment K-SARA scores may suggest that the MSC therapy can have a neuroprotective effect and that stem cell therapy may serve as a potential therapeutic option for degenerative cerebellar ataxia.
VESTIBULO-OCULAR REFLEX IN SPINOCEREBELLAR ATAXIA: DOES IT HAVE A DIFFERENTIATING VALUE?

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Background and Aims:: The differential diagnosis of spinocerebellar ataxia (SCA) is often difficult and usually dependent upon genetic testing since the clinical phenotypes of SCAs considerably overlap. SCA may present VOR impairments, though the previous studies have shown inconsistent results. We aimed to assess VOR of SCA patients with various subtypes using video head impulse test (HIT) device, and to determine whether they have differentiating value.

Methods:: 25 genetically confirmed SCA patients (SCA2=5, SCA3=3, SCA6=9, SCA7=8) were enrolled. Baseline demographics, vestibular performance, and combined ocular motor dysfunctions were investigated. Furthermore, correlation analyses were performed between clinical parameters and the VOR gains. Normative data were obtained from 40 age-matched healthy control.

Results:: Compared to normal control, the VOR gains were spared in SCA2, but globally decreased in SCA3. In vertical canals, SCA6 showed posterior canal-dominant gain impairments, but SCA7 exhibited impaired gains in both anterior and posterior canals. The gains for the horizontal canals in SCA6 and the vertical canals in SCA7 were negatively correlated with disease severity. Saccadic slowing associated with absent gaze-evoked nystagmus were prominent in SCA2 and SCA7. Spontaneous and evoked nystagmus were common in SCA6. Pursuit and optokinetic nystagmus impairments were frequent regardless of subtypes.

Conclusions:: VOR impairments are common in SCA, but their patterns were various according to the subtypes. Distinctive VOR performance for each subtype using video HITs may aid the differential diagnosis of the SCA genotypes and may lead to a better understanding of the neuropathology.
CEREBELLO-SPINAL STIMULATION IN NEURODEGENERATIVE ATAXIA: MOTOR AND COGNITIVE OUTCOMES.

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Background and Aims:: In this randomized, double-blind, sham-controlled trial, followed by an open-label phase, we investigated whether treatment with cerebello-spinal transcranial direct current stimulation (tDCS) could improve both motor and cognitive symptoms in patients with neurodegenerative ataxia, a still orphan disorder of any pharmacological intervention.

Methods:: Sixty-one patients were randomized in two groups for the first controlled phase. At baseline (T0), Group 1 received placebo stimulation (sham tDCS) while Group 2 received anodal cerebellar tDCS and cathodal spinal tDCS (real tDCS) for 5 days/week for two weeks (T1), with a 12-week (T2) follow-up. At the 12-week follow-up (T2), all patients received a second treatment of real tDCS for 5 days/week for two weeks, with a 14-week (T3), 24-week (T4), 36-week (T5) and 52-week follow-up (T6). At each time point, a clinical, neuropsychological and neurophysiological evaluation was performed. Cerebellar-motor cortex connectivity was evaluated using transcranial magnetic stimulation (TMS).

Results:: We observed a significant improvement in all motor scores, in cognition, in quality-of-life scores, in motor cortex excitability and in cerebellar inhibition after real tDCS compared to sham stimulation and compared to baseline (T0), both at short and long-term. We observed an addon-effect after two repeated treatments with real tDCS compared to a single treatment with real tDCS.

Conclusions:: Multiple sessions of cerebello-spinal tDCS repeated every 3 months, are an effective, non-invasive, painless, and easy to perform treatment to be considered in the spectrum of neurodegenerative ataxias, capable of improving both motor and cognitive functions with long-lasting effects.
Background and Aims:: Introduction Neuro-degeneration with brain iron accumulation (NBIA) is where early deposition of iron in the basal ganglia and the other deep grey matter is characteristically associated with movement disorders. Spinocerebellar ataxia (SCA) is characteristically a neurodegenerative disorder predominantly affecting the cerebellum and the cortico-spinal tracts. Rarely excess iron accumulation is reported in long standing SCA patients. We report a case of genetically proven SCA38 with evidence of excess iron deposition in the basal ganglia similar to a NBIA.

Methods:: Case report A 38 year old woman presented with difficulty in walking and maintaining her balance for 3 years. She didn’t complain of any sensory symptoms and denied any defect in the sense of smell or hearing. On examination she was ataxic and bradykinetic with parkinsonism. There was gaze evoked horizontal nystagmus. Appendicular rigidity was prominent with exaggerated reflexes and extensor planter responses. She didn’t have any evidence of pes cavas. She did not have KF rings. Ceruloplasmin, serum cooper, TSH, Serum Ferritin were normal.

Results:: MRI showed evidence of brain iron accumulation with prominent cerebellar atrophy. Her genetic studies showed heterozygous ELOVL5 gene mutation due to c.304C>T mutation characteristic of SCA 38.

Conclusions:: SCA38 is characterized by slowly progressive ataxia with prominent cerebellar signs. Evidence of brain iron accumulation which normally occurs with NBIA and Wilson’s disease (WD) is unusual in SCA. Brain iron accumulation was previously reported only in cases of SCA15. It has never
been reported before in SCA 38. A genetic evaluation in such cases is of paramount importance to make an accurate diagnosis distinguishing SCA from NBIA and WD.
Background and Aims:: Paraneoplastic cerebellar degeneration is rare and can be the presenting feature of an underlying malignancy

Methods:: A 75 year old retired police officer with type 2 diabetes and hypertension presented with gradually worsening unsteadiness since 2 weeks. He was a heavy smoker. He gave a history of recent onset loss of weight and loss of appetite. He denied any respiratory symptoms. Physical examination revealed bilateral cerebellar signs. He was wasted but didn’t have any other significant findings during the examination. His MRI brain was significant for marked cerebellar atrophy. Contrast enhanced CT scan of the chest showed 2 cm nodule in the right middle lobe. CT guided biopsy was performed which confirmed the diagnosis of small cell carcinoma of the lung. Anti neuronal antibodies were remarkable for a positive anti Hu antibody. His thyroid functions, serum vitamin B12 levels were normal. He was referred to oncology team following the diagnosis.

Results:: Paraneoplastic cerebellar ataxia is one of the most common paraneoplastic syndromes. Its characterized by rapid development of severe pancecerebellar dysfunction. Since it can precede the presentation of neoplasms by several months to years, a high degree of suspicion is needed. Lung, testicular, ovarian, breast carcinoma, Hodgkin’s lymphoma are the common types associated with paraneoplastic cerebellar degeneration.

Conclusions:: Paraneoplastic cerebellar degeneration should be considered in elderly patients presenting with constitutional symptoms and ataxia.
ANTI-MGLUR1 MEDIATED CEREBELLAR ATAXIA CASE REPORT & REVIEW OF LITERATURE

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Background and Aims: Immune-mediated neurological disorders literature is evolving like no other field of neurological illnesses. Many new antibodies and disorders have been described in the last decade. The cerebellum is one of the brain structures susceptible to these immune-mediated pathologies and anti-metabotropic glutamate receptor 1 (mGluR1) antibodies have a predilection to cerebellar tissue. Cerebellar ataxia associated with anti-mGluR1 is a rare autoimmune-mediated disorder. As about one-quarter of the reported cases have an associated malignancy, investigating for occult malignancies is important. We aim to describe the first case of anti-mGluR1 antibody-mediated cerebellar ataxia in the Middle East.

Methods: Case-report & review of literature

Results: We describe a case of non-paraneoplastic cerebellar ataxia associated with anti-mGluR1 antibodies in a 56-year-old female. She presented with cerebellar ataxia, dysarthria, tremors, and diplopia following a febrile illness. CSF analysis showed lymphocytic pleocytosis with positive oligoclonal bands. Brain MRI was initially unremarkable and six months later showed cerebellar atrophy. Serum and CSF anti-mGluR1 antibodies were positive. She was treated with pulse intravenous methylprednisolone, intravenous immunoglobulin (IVlg), and plasma exchange (PLEX) as acute treatment. For maintenance, she received IVlg, PLEX, rituximab, and azathioprine over the course of 3 years. She improved and is in remission until now; follow-up extensive workup showed no occult malignancy.

Conclusions: Anti-mGluR1 Cerebellar Ataxia is an immune-mediated disorder that warrants early diagnosis to initiate therapy promptly with the goal to achieve a better outcome. Testing for mGluR1 antibodies should be considered in any acute or subacute cerebellar ataxia especially when it follows a prodrome of febrile illness.
CEREBELLAR COGNITIVE AFFECTIVE SYNDROME IN PATIENT WITH CEREBELLAR INFARCTION

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Background and Aims:: Schmahmann (1998) described the ‘cerebellar cognitive affective syndrome’, (CCAS) reporting impairments in executive functions, disturbances in spatial cognition, language deficits and personality changes in subjects with cerebellar pathologies. the current CCAS literature consists of only small series of patients that are frequently biased by patient selection rather than consecutive inclusion. and is clear that stroke in the anterior lobe for occlusion of Anterior Inferior Cerebellar Artery (AICA) produced the motor syndrome but not the CCAS, whereas stroke in the posterior lobe posterior Inferior Cerebellar Artery (PICA) produced the CCAS. however is controversial the role of the Superior Cerebellar Artery (SCA) that included largest part of the deep white matter with most of or the whole dentate nucleus.

Methods:: revision of clinical record of case of a 56-year-old man with complete clinical, neurocognitive and imagenological evaluation is presented
Results: A cerebelar stroke for basilar-vertebral atheromatosis with MRI evidence show extensive infarction of the bilateral SCA and the left PICA without encephalic supratentorial damage Has severe motor cerebellum syndrome with BARS score of 17/30 and cognitive deficit in language functions, attention, visual construction and behavioral manifestations such as apathy. CCAS scale is applied with total score of 22/120 and 8/10 failed item

Conclusions: this case meets diagnostic criteria of CCAS with cognitive profile consistent with cognitive deficits in the stroke of PICA without cerebral compromise, also in this case the bilateral injury of SCA
probably contributes at the multidimensional cognitive deterioration for the damage of the cortical efferent pathways in the white matter and deep cerebellar nuclei.
A GUIDELINE ON THE DIAGNOSIS AND TREATMENT OF CHILDREN WITH ATAXIAS

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Background and Aims:: The activities of the project “Pediatric ataxias and Public Health: epidemiological studies and disease registry, characterization of genetic determinants and implementation of protocols for diagnosis, management, and rehabilitation using innovative low cost, widely accessible technologies”, funded by the Ministry of Health, included the production of a guideline (GL) on the diagnosis and treatment of children with ataxias.

Methods:: The GL was produced using the GRADE approach. A systematic review (SR) of the literature was performed to gather available evidence on each clinical question included in the scope of the GL. Results from the SR were reported in summary of findings (SoF) tables and the multidisciplinary panel (MP), after discussing the evidence, produced clinical practice recommendation (CPR) along with their respective evidence-to-decision tables.

Results:: The GL included 28 clinical questions (2 on acute ataxias, 10 on the diagnosis of chronic ataxias, 12 on the pharmacological and habilitative/rehabilitative treatment of chronic ataxias, and 2 on care models). Specific SRs were carried out for each question. Selected evidence was qualitatively assessed and SoF tables were built, including a judgement of each body of evidence. Discussion with the MP lead to the definition of 39 CPR and 7 research recommendations. Following the NICE and the European Pathway association (EPA) models, a care pathway was also produced, in the form of an interactive pdf. An informative leaflet was also produced.

Conclusions:: To our knowledge, this is the first guideline produced using a standardized methodology and including evidence-based recommendation on these rare diseases.
METABOLIC IMAGING PATTERNS IN CEREBELLAR ATAXIA SYNDROMES

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Background and Aims:: To elucidate the patterns of characteristic hypometabolism on 18F-FDG PET/CT in cerebellar ataxia syndromes.

Methods:: A retrospective analysis of 70 patients of clinically diagnosed ataxia syndrome was done. All the subjects were clinically analyzed and were further segregated into hereditary and acquired sub groups of SCA (n=10), MSA-C (n=40), Normal pressure hydrocephalous (NPH) (n=20) and 5 subjects diagnosed with autoimmune cerebellar degeneration. All the subjects underwent 18F-FDG PET/CT and 99mTc TRODAT-1 SPECT studies. The FDG uptake patterns were recorded and areas of hypometabolism that were two standard deviations from the mean were considered as abnormal.

Results:: 99mTc TRODAT-1 scan was abnormal in all the subjects of suspected MSA-C, establishing degenerative Parkinsonism. 99mTc TRODAT-1 scan was normal in all subjects of SCA and NPH. On FDG PET, the subjects of SCA showed diffuse mild to moderate hypometabolism involving the bilateral cerebellar hemispheres, cerebellar peduncles, sensori-motor and insular cortices, whereas the subjects of MSA-C had diffuse moderate to severe hypometabolism involving the bilateral cerebellar cortices, cerebellar vermis, sensori-motor cortices, basal ganglia and brain stem. The subjects with NPH showed global cortical and sub cortical hypometabolism. Among the 5 subjects with autoimmune cerebellar degeneration, 3 had anti-yo positive para neoplastic degeneration and showed diffuse cerebellar hypometabolism, while 2 had anti-GAD positive autoimmune encephalitis with areas of hypometabolism and hypermetabolism.

Conclusions:: Characteristic patterns of hypometabolism may help in differentiation of the cerebellar ataxia syndromes. 99mTc TRODAT-1 SPECT helps in confirmation of degenerative Parkinsonian disorder like MSA-C, from other degenerative ataxia syndromes.
FREQUENCY AND FEATURES OF SPINOCEREBELLAR ATAXIAS IN BRAZILIAN PATIENTS FROM RIO DE JANEIRO

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Background and Aims: Previous studies show geographic and ethnic differences in the frequency of hereditary ataxias worldwide. Few data about spinocerebellar ataxias (SCA) are available in Rio de Janeiro (RJ), in the Southeast region, where there is a high proportion of Afro-descendants in the population. The aim of this study is to describe the frequency and features of SCAs in a cohort of patients from RJ.


Results: 147 patients were identified. SCA 3 was the most frequent type (107). Less frequent types were SCA 7 (9), SCA 2 (5), SCA 1, SCA 6 and SCA 8 (2) and SCA 10 (1). The genetic tests were negative in 19 cases. Extra cerebellar symptoms were: dysphagia, pyramidal syndrome, neurogenic bladder, ophthalmoplegias, extra pyramidal syndrome, peripheral neuropathies, epilepsy, and visual impairment. Brain MRI was performed in 106 patients. Cerebellar atrophy was the most frequent finding (88.6%) followed by brain stem atrophy (33%), cross sign (15%), and brain atrophy (10.3%). Normal MRI (9.4%). ENMG performed in 55 SCA3 were abnormal in 74.3%, polyneuropathy (50.9%), motor neuronopathy (40%) and radiculopathy (18.5%). CAG repetitions in SCA3 varied between 50 and 78 (mean = 65).

Conclusions: SCA3 is the most frequent type of spinocerebellar ataxia in Rio de Janeiro, similar to Caucasian populations. Cerebellar atrophy and extra cerebellar neurological manifestations occurred in most cases.
PHENOTYPIC CHARACTERISTICS OF PATIENTS WITH ARSACS FROM SOUTH INDIA

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Background and Aims:: Early onset autosomal recessive ataxias consist of numerous entities with distinctive phenotypes. In 1978, a spastic ataxic syndrome was reported from Quebec, which was acronymized as ARSACS; autosomal recessive spastic ataxia of Charlevoix-Saguenay. We aim to describe a cohort of patients with ARSACS from a South India.

Methods:: We conducted a retrospective review in a single neurology unit of a university teaching hospital. Clinical and electrophysiological details of patients diagnosed with ARSACS based on clinical and characteristic imaging features i.e., linear T2 hypointensities in the pons and anterolateral thalamic hyperintensities were recorded (n=7, M:F=4:3).

Results:: The mean age at onset was 5.8±4.6 years (range: 2-13 years). Four individuals were born to consanguinity. The median time to diagnosis from onset was 18 years (range: 5-26 years). Initial/referral diagnosis was ataxic cerebral palsy (n=2), hereditary motor neuropathy (n=2), spastic ataxia syndrome (n=2) and unexplained gait difficulty (n=1). All patients had motor developmental delay at onset of illness which was subsequently followed by gait difficulty. Though spasticity was observed in only two patients, all the patients except one, had extensor plantar response. Three patients had hyper-myelinated retinal nerve fibers. Nerve conduction studies were abnormal in all the patients. Genetic testing was done in two individuals, both harbored homozygous pathogenic mutations in the SACS gene.

Conclusions:: ARSACS is a slowly progressive autosomal recessive ataxia with pathognomonic imaging findings. Early diagnosis can facilitated by careful characterization of phenotype and review of MRI.
AN UPDATE ON PERIPHERAL BLOOD NEUROFILAMENTS IN THE DIAGNOSIS OF MULTIPLE SCLEROSIS

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Background and Aims:: Background: Imagine being able to tell “there is no inflammation or degeneration in your nervous system currently”. Aims: The future of neurofilaments in RRMS and whether they can be included in our routine clinical practice.

Methods:: A total of 440 journal articles were obtained, after 2 screenings 5 studies were extracted, a total of 891 patients studied.

Results:: “Serum neurofilament light chain as a predictive marker in patients after first demyelinating event suggestive of multiple sclerosis”. Concluding that high levels of neurofilaments during the first demyelinating event are suggestive of MS and are associated with greater activity, low levels of neurofilaments are related to NEDA 3, up to 4 years. “Serum neurofilament light chain levels in patients with presymptomatic multiple sclerosis”. Concluding that the levels of neurofilaments can be found elevated up to 6 years before diagnosis, their maximum elevation at the time of clinical debut. “Prognostic value of serum neurofilaments in patients with clinically isolated syndromes”. Concluding that the levels of neurofilaments have a prognostic value in patients with clinically isolated syndrome, the low levels can reduce up to 3 times the risk of developing MS, the increase in the levels represent activity and the levels maintained constant damage. “Serum neurofilament light chain levels are increased in patients with a clinically isolated syndrome”. Concluding that neurofilament levels are elevated in patients with clinically isolated syndrome. “Neurofilament-light chain levels are predictive of ongoing disease activity in radiologically isolated syndrome”. Concluding that neurofilaments are an independent factor to predict disease activity.

Conclusions:: In the previous
BILATERAL OPTIC ATROPHY WITH PITUITARY FAILURE: A RARE DIFFERENTIAL

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Background and Aims: Bilateral optic atrophy together with pituitary failure, likely related to IgG4-related disease is a rare clinical entity.

Methods: A 35-year-old male presented with progressively worsening visual loss of the right eye and was found to have asymmetrical, bilateral optic atrophy, affecting the right eye more than the left. He was noted to have short stature and a lack of secondary sexual characteristics with low testicular volume. He also reported polyuria since 13 years of age. Further assessment showed hypopituitarism and diabetes insipidus. Magnetic resonance imaging of the brain and orbits showed an asymmetrical contrast-enhancing soft tissue lesion in both cavernous sinuses with extension into both orbital apices and involvement of intra-cranial optic nerves and the chiasm with dural thickening and a hypoplastic pituitary gland. Evaluation for tuberculosis and sarcoidosis were negative. Biopsy of the lesion showed lymphocytes, plasma cells and some neutrophils with areas of sclerosis, without necrosis or granuloma formation. IgG4-related disease was considered likely but not confirmed due to the non-availability of the appropriate staining. The serum IgG4 levels were normal. He was treated with hormonal replacement and high dose steroids. Due to inadequate clinical and radiological response, IV rituximab was given. This led to clinical improvement with complete resolution of diabetes insipidus but his vision remains unaltered without a significant radiological improvement at 2 months post-rituximab.

Results:
Conclusions: This case highlights the necessity of entertaining alternate diagnoses such as IgG4-related disease, in patients with enhancing soft tissue lesions involving the CNS negative for tuberculosis and sarcoidosis.
SAFETY OF ECULIZUMAB IN NMOSD AND MG: ANALYSIS OF THE PHASE 3 STUDIES PREVENT AND REGAIN, AND THEIR EXTENSIONS

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Background and Aims:: Eculizumab (a terminal complement inhibitor) demonstrated efficacy in reducing relapse risk and eliciting clinical improvements in the phase 3, randomised, double-blind PREVENT (NCT01892345) and REGAIN (NCT01997229) studies and their open-label extensions (NCT02003144 and NCT02301624, respectively) in aquaporin-4 immunoglobulin G-positive neuromyelitis optica spectrum disorder (AQP4+ NMOSD) and acetylcholine receptor antibody-positive generalised myasthenia gravis (AChR+ gMG), respectively. The aim of this analysis was to compare infection rates for eculizumab vs placebo according to number of concomitant immunosuppressive therapies (ISTs) during these studies. Eculizumab is not reimbursed for neurology indications in Italy as of April 2021.

Methods:: Patients were randomised to eculizumab or placebo. Post hoc analysis examined infection rates overall and by number of baseline ISTs.

Results:: Infection rates/100 patient-years for eculizumab vs placebo in NMOSD and gMG, respectively, were: no IST, 176.1 vs 192.2 and 236.8 vs 305.6; 1 IST, 171.5 vs 154.1 and 228.8 vs 253.1; 2 ISTs, 186.7 vs 238.2 and 170.5 vs 192.5; ≥3 ISTs (gMG only), 97.5 vs 100.1. Serious infection rates/100 patient-years were: no IST, 2.3 vs 8.0 and none observed; 1 IST, 11.2 vs 7.0 and 16.2 vs 34.5; 2 ISTs, 14.8 vs 47.6 and 13.4 vs 24.1; ≥3 ISTs (gMG only), 13.9 vs 0.0. One patient with gMG (2 ISTs) had meningococcal meningitis that resolved with antibiotics and eculizumab was resumed.

Conclusions:: In AQP4+ NMOSD and AChR+ gMG, infection rates were similar in eculizumab and placebo groups, regardless of concomitant IST, and were consistent with eculizumab’s established safety profile. This study was funded by Alexion Pharmaceuticals, Inc.
Background and Aims: Hashimoto’s Encephalopathy (HE), is a rare autoimmune disorder to be considered in patients with neuropsychiatric symptoms accompanied by normal or nonspecific brain MRI, LCR findings and thyroid function or mild hypothyroidism, increased serum levels of thyroid peroxidase antibodies (TPOAb), and response to steroids. We describe the case of a 68-years old caucasian female without previous psychiatric history conducted to Emergency Care in February 2020 for recently debuted confusion, visual hallucinations and cleanliness delusions in response to SARS-COV2 pandemic.

Methods: We found TSH elevation (38.05 μUI/mL) with negative brain CT. EEG presented diffuse 2-4 Hz activity. LCR findings were negative for infections. Brain MRI was inconsistent. We started levothyroxine replacement. At EEG reappeared an alpha activity. TSH began to descend. TPOAb were at a very high titer (>600 U/mL). We started oral prednisone with initial neuropsychiatric improvement. Patient rapidly got again worse in psychiatric aspects and presented also extrapiramidal signs. Antibodies against cell-surface, synaptic and onconeural proteins were absent. CT total body was inconsistent. 18PDG-PET was negative. Levels of beta amyloid, 14-3-3protein, tau and phospho-tau in LCR were normal. Brain PET demonstrated an hypometabolism in frontotemporoparietal bilateral regions. At psychometric tests patient presented a multi-domain disorder. We treated her with high dose intravenous corticosteroids followed by an immunoglobulins cycle.
Results:: At follow-up extrapiramidal and psychiatric disorders got slowly better. At control psychometric tests and cerebral PET patient improved. She is performing 18PDG- PET every 6 months to exclude an underlying paraneoplastic syndrome.

Conclusions:: Hashimoto’s Encephalopathy seems to respond to steroids and immunoglobulins therapy.
Background and Aims:: SARS-CoV-2 infection is now known to be associated with a wide spectrum of neurological autoimmune syndromes, in some cases responding to immunotherapies, arising during or after the infection. Whether molecular mimicry or other immune stimulation may induce an aberrant delayed autoimmune response is still to be established.

Methods:: Case Report

Results:: A 71-year-old man with no previous medical history apart from mild COVID-19 pneumonia 3 month earlier, sought medical attention for a subacute onset of diplopia in left gaze, general malaise and fatigue. MRI was characterized by bilateral FLAIR hyperintensities with punctate, perivascular and confluent post-gadolinium enhancement in the pons, mesencephalon, hypothalamus, internal capsules and right hippocampus. Repeated cerebrospinal fluid analysis were normal (2 cells/µL), with no evidence of oligoclonal bands or atypical cells. Screening panel for autoimmune and infectious aetiologies was negative. Whole-body contrast-enhanced CT was unremarkable. Stereotactic temporal lobe brain biopsy showed aspecific chronic lymphocytic perivascular inflammation. Partial spontaneous remission of symptoms occurred within few weeks. He was then treated with intravenous high-dose methylprednisolone with almost complete enhancement regression on MRI. Collected data were suggestive of CLIPPERS with diffuse bilateral supratentorial involvement. The patient started daily oral steroid tapering and monthly cycles of intravenous cyclophosphamide with persistent clinical and neuroradiological stability.

Conclusions:: CLIPPERS is a rare diagnosis and to the best of our knowledge, this is the first time it was reported after COVID-19 disease. Even though a case report is not enough to suggest a causal link, future reports could support this possibility.
A RARE CAUSE OF DRUG INDUCED MONONEUROPATHY

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Background and Aims:: Drug-induced mononeuropathy is a common and painful condition seen with use of chemotherapeutic agents, antimicrobials and anticonvulsants. It takes weeks to months to set in. Churg Strauss Syndrome (CSS) is primarily a disease of middle age and its presentation in childhood is rare. We hereby present a rare case of an adolescent female presenting with mononeuropathy which later turned out to be a part of eosinophilic granulomatosis with polyangiitis or CSS precipitated by prolonged use of leukotriene receptor antagonist.

Methods:: 16 year old female child presented with complaints of rash and swelling over legs and arthralgia for last 7 days. She also had severe pain and numbness in right foot. Child had been diagnosed with bronchial asthma one year back for which she took montelukast. A nerve conduction velocity study was done which showed evidence of sensory neuropathy in right sural nerve. The complete blood counts consistently showed more than 70% eosinophils. Total IgE levels were elevated and HRCT chest showed bronchiectasis. Skin biopsy results revealed leukocytoclastic vasculitis with perivascular eosinophils. With the diagnosis of CSS child was started on oral steroids and montelukast was discontinued. pANCA and cANCA levels were negative.

Results:: After starting corticosteroids, neuropathy improved and eosinophil count was reduced to 8%. She was discharged on oral corticosteroids and is currently on regular follow up.

Conclusions:: With rampant use of LTRAs in asthma, primarily cough variant asthma, among physicians, we should be watchful for such immune mediated phenomenon as there could be life threatening end organ involvement.
PACHYMENINGITIS IN GRANULOMATOSIS WITH POLYANGIITIS: A CASE REPORT

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Background and Aims:: Granulomatosis with polyangiitis (GPA; formerly called Wegener's) is a rare small to medium sized necrotizing vasculitis. Neurological manifestations include cranial and peripheral neuropathies whereas meningeal and central nervous system (CNS) involvement is unusual.

Methods:: Case report

Results:: We describe the case of a 51-year-old woman with subacute complete visual loss in her left eye following one month history of progressive visual impairment associated with nausea, vertigo and headache. Her recent past medical history included recurrent otitis, mastoiditis and chronic sinusitis. Neurological examination showed multiple cranial neuropathies: right trigeminal hypoesthesia, left abducens nerve palsy, peripheral facial nerve palsy, right hearing loss. Brain MRI showed contrast-enhanced pathological tissue in the right medium-inner ear involving also the petrous temporal bone and vascular structures, multifocal pachymeningitis (PM) and extensive brain edema. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were elevated. Lumbar puncture was negative for infection and only showed a mildly elevated CSF protein and cell count. P-ANCA antibodies directed against myeloperoxidase were positive. Finally, a dural biopsy revealed numerous multinucleated giant cells and necrotizing vasculitis. Initially she received standard therapy with corticosteroid with significant improvement, then rituximab was started.

Conclusions:: Pachymeningitis is a rare manifestation of GPA. Our case presented with classical symptoms of otitis, mastoiditis and chronic sinusitis, but was followed by multiple cranial neuropathies and significant meningeal-CNS involvement short after. A dural biopsy was therefore necessary to confirm the clinical diagnosis for a timely therapy.
Background and Aims:: Multiple Sclerosis (MS) and Psoriasis are both autoimmune T cell-mediated diseases, with similarities in genetic risk variants and inflammatory pathways. So far, limited evidence is available on the relationship between the two diseases and on the impact of one disease on the course of the other.

Methods:: We report the case of three cases of MS with psoriasis and correlate our findings with a brief review of literature, to investigate the potential relationship between psoriasis and MS.

Results:: We present the case of three multiple sclerosis patients with psoriasis comorbidity. No family history of psoriasis was found. The median age of onset of MS was 22 years old. Psoriasis preceded MS in only one case, and the duration between the diagnosis of psoriasis and the onset of MS was 15 years. The other two patients developed psoriasis few months after initiation of Interferon-B therapy. Nonetheless, psoriasis lesions were not severe (less than 3% of the body is affected), and did not warrant treatment interruption. All the patients were treated with topical corticosteroids with a favorable outcome. The three patients had slower progression of disease, as manifested by a longer time to second relapse and a longer time to significant neurological disability scores.

Conclusions:: Although psoriasis has been reported as an undesirable effect of interferon-Beta therapy, the common genetic linkages in these two diseases cannot be denied. Further studies are warranted to establish the mechanisms underlying this relationship and its potential clinical and therapeutic consequences.
CLINICAL VARIABILITY AND THE ROLE OF DIAGNOSTIC CRITERIA OF CEREBRAL AMYLOID ANGIOPATHY-RELATED INFLAMMATION (CAA-RI): A CASE SERIES.

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Background and Aims:: Cerebral amyloid angiopathy (CAA) is usually a cause of hemorrhagic stroke. Rarely it could be complicated by an inflammatory brain disease called CAA-related inflammation (CAA-ri) as a consequence of amyloid-β auto-antibodies production. Symptoms and their onset vary widely among patients, from headache to coma, and from chronic to acute onset. In the past, diagnosis was possible only performing a brain biopsy. Recently, in order to avoid procedural risks of a brain biopsy and to accelerate the diagnostic process and consequent treatment, clinicoradiological diagnostic criteria were proposed. Among all proposed therapies, high dose corticosteroids have shown to be the most effective.

Methods:: Three cases of CAA-ri are described. The first case is a 77-year-old woman who presented a subacute cognitive impairment. Her clinical conditions rapidly deteriorated leading to fatal outcome 11 days after admission. Autopsy posed the diagnosis of CAA-ri. The second and the third patients were an 81-year-old man hospitalized for a generalized epileptic seizure and an 80-year-old woman with a recent history of nocturnal headache. After a brain MRI and exclusion of other causes, a diagnosis of probable CAA-ri was made according to the clinicoradiological criteria and a corticosteroid treatment was immediately begun. Both patients fully recovered after
treatment.

**Results:** In the second and third case, application of diagnostic criteria permitted a faster treatment and a better outcome.

**Conclusions:** CAA-ri may present with a wide range of symptoms and severity. The application of clinicoradiological criteria to diagnose CAA-ri has allowed a faster diagnosis and a faster treatment with a consequent improved outcome.
Background and Aims:: Anti-GFAP astocytopathy is a rare and relatively new disease. Neuropathology has been hitherto only described in 4 cases. We report one other case, and discuss the uniqueness of the neuropathology in these cases based on a potential second case.

Methods:: Case report.

Results:: This 64-year-old right-handed gentleman had at presentation a 2 month history of light-headedness, and one month of minor cognitive changes and unsteadiness of gait. An MRI scan revealed left fronto-parietal deep white matter T2 signal abnormality and mild restricted diffusion without mass effect. Numerous serologic and CSF investigations suggested inflammatory etiology but were otherwise unrevealing. The patient continued to have progressive cognitive decline and worsening disequilibrium. A white matter biopsy showed non-neoplastic mononuclear perivascular infiltrates with fairly frequent eosinophils and plasma cells, and diffuse gliosis with non-monoclonal/neoplastic plasma cells diffusely in the white matter. There were some clusters of macrophages surrounding astrocytes, but without demyelination. A concomitant CSF sample tested positive for anti-GFAP antibodies. Patient was given high dose steroids and significantly improved. In 2018 we saw a patient with similar clinical history, MRI scan, and brain biopsy findings. CSF was tested for anti-GFAP antibodies at the time and was negative. This patient passed away and a final diagnosis was never reached.

Conclusions:: White matter parenchymal gliosis with non-neoplastic parenchymal plasma cell infiltrates in the right clinical setting and imaging results may be a strong pointer towards autoimmune GFAP astrocystopathy. However, based on our second patient it may well be that this neuropathological vignette is not entirely specific.
KAPPA INDEX IN PATIENTS WITH AUTOIMMUNE ENCEPHALITIS

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Background and Aims:: The diagnosis of autoimmune encephalitis (AE) can be complex and is supported by the presence of inflammatory changes in the cerebrospinal fluid (CSF), including intrathecal immunoglobulin synthesis (IS). Aim was to calculate the kappa index (CSF/serum kappa free light chain-KFLC-divided by CSF/serum albumin ratio), as a marker of IS, in patients with a diagnosis of AE or possible AE according to the Graus criteria.

Methods:: CSF/serum KFLC were tested using Freelite kits (The Binding Site Group, UK) on samples stored after the diagnostic spinal tap of patients with AE/possible AE between 2009 and 2019.

Results:: We included 31 patients:22 with AE (7 anti-LGI1, 6 anti-NMDAR, 2 anti-CASPR2, 2 anti-GAD, 2 anti-Ma2, 1 anti-VGKC, 1 anti-GABAbR-positive and one antibody-negative) and nine with possible AE. Eight AE (36%) and one possible AE patient (11%) had CSF-restricted oligoclonal bands (OCB) and three patients each in the AE (14%) and possible AE group (33%) had pleocytosis (>5 cells mm3). Kappa index had a mean value of 9.1(±13.3) in AE and 0.6(±1.2) in possible AE patients. Among AE patients, it was highest in anti-NMDAR (12.6±19.5) and lowest in anti-LGI1 encephalitis (0.87±1.6). Kappa index was ≥3 in 13 (59%) AE and in one (11%) possible AE patient. In two AE patients (9%) an elevated kappa index was the only abnormal CSF inflammatory marker.

Conclusions:: If confirmed in other large series, kappa index might integrate OCB and pleocytosis as a supportive biomarker of neuroinflammation among the Graus criteria.
FULMINANT GUILLAIN-BARRÉ SYNDROME POST-HEMORRHAGIC STROKE: TWO CASE REPORTS.

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Background and Aims:: Guillain-Barré syndrome (GBS) is an acute, immune-mediated inflammatory peripheral polyneuropathy characterized by ascending paralysis. Most of the GBS cases follow gastrointestinal or chest infections. Some patients have been reported either following or concomitant with head trauma, neurosurgical procedures, and rarely Hemorrhagic stroke. The exact pathogenesis is not entirely understood. However, blood-brain barrier damage may play an essential role in triggering the autoimmune activation that leads to post-stroke GBS. Here, we present two cases of fulminant GBS following hemorrhagic stroke to remind the clinicians to be aware of this rare treatable complication if a stroke patient developed unexplainable flaccid paralysis with or without respiratory distress.

Methods:: Case report and literature review.

Results:: Here we report two cases who were diagnosed with GBS following hemorrhagic stroke. The first patient developed GBS after endovascular mechanical thrombectomy for acute ischemic stroke complicated by a hemorrhagic transformation. While the second patient developed GBS after hematoma evacuation.

Conclusions:: These case studies highlighted the importance of considering GBS in the differential diagnosis of patients with flaccid quadripareisis and respiratory failure after a hemorrhagic stroke. It may explain those patients’ clinical progression when early therapy could make a difference in their prognosis and outcome.
Background and Aims:: Primary CNS vasculitis is a rare and poorly understood inflammatory disorder of blood vessels of brain and spinal cord presenting mainly as headaches and recurrent focal neurological deficits. Involvement of cauda equina is rarely reported which makes it even more challenging to diagnose this disease.

Methods:: We present a 15-year-male who presented with history of headache since 8 months and recurrent seizures since 6 months with right hemiparesis since 5 days with clinical examination further showing absent ankle jerks bilaterally. MRI brain had shown miliary perivascular enhancement of brain with multiple hemorrhages and enhancement of cauda equina nerve roots. Patient was further worked up for other secondary causes.

Results:: CSF showed lymphocytic pleocytosis with increased protein with negative workup for secondary causes of vasculitis. Leptomeningeal and cortical biopsy had confirmed diagnosis of primary CNS vasculitis. Patient was further started on immunomulation with partial recovery of symptoms and resolution of imaging findings.

Conclusions:: This report emphasizes the awareness of this varied clinical spectrum of cauda equina involvement in Primary CNS vasculitis and highlights importance of recognition of miliary enhancement on MRI images of brain to suspect and further facilitate diagnostic work-up.
B CELL RELATED PREDICTIVE BIOMARKERS OF TREATMENT RESPONSE IN MYASTHENIA GRAVIS

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Background and Aims:: Myasthenia Gravis (MG) is a B cell-mediated autoimmune disease characterized by muscle weakness and fatigability, mostly associated to antibodies against the acetylcholine receptor (AChR). MG patients are chronically treated by immunosuppressants and 10-15% are treatment refractory. The purpose of our study is to identify changes in B-cell subsets that could predict treatment response in MG subgroups with different treatment-related status, with the aim of improving MG management, leading to personalized therapy.

Methods:: Peripheral blood mononuclear cells (PBMCs) were isolated from 79 AChR-MG patients for the characterisation of transitional (CD19+CD20+CD24+CD38+), naïve (CD19+CD20+IgD+CD27-), double negative (CD19+CD20+IgD-CD27-), unswitched memory (CD19+CD20+IgD+IgM+CD27+), switched memory (CD19+CD20+IgD-CD27+IgG+), plasmablasts (CD19+CD27+CD38+) by multicolour flow cytometry.

Results:: Thirty/66(46%) patients were women and mean age at onset was 48 years. At sampling, 15/79(19%) patients were immunotherapy- naïve, 38/79(48%) were immunotherapy-responders, 13/79(16%) were refractory to standard immunotherapy and 25/79(36%) were in clinical stable remission (CSR). The frequency of total B-cells did not differ among the clinical subgroups. Naïve B-cells were lower (Fig.1A) in immunotherapy-responders compared to immunotherapy- naïve(p=0.005), refractory and patients in CSR(p=0.009). Transitional B-cells were increased in refractory MG (Fig.1B) compared to immunotherapy- naïve(p=0.01) and responders(p=0.029). Surprisingly, plasmablasts were lower in refractory patients than immunotherapy- naïve patients (Fig.1C)
Conclusions: The persistence of transitional B-cells, rather than antigen experienced B-cells, might predict unresponsiveness to immunotherapy in a subgroup of patients. In these cases, B cell-directed therapies could restore the balance between regulatory and inflammatory B-cells in the pre-germinal compartment.
AUTOIMMUNE ENCEPHALITIS: ANTIBODIES TO NEUROTRANSMITTERS, ION CHANNELS, TUMOR ANTIGENS. WHAT NEXT?

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**Background and Aims:** Autoimmune encephalitis (AE) is relatively rare and recently described group of diseases involving autoantibodies (AB) directed against synaptic and neuronal cell surface antigens. AE includes wide range of neurological symptoms. Sensitive and specific diagnostic tests, such as cellular analysis, are of paramount importance for detecting neuronal cell surface AB, in cerebrospinal fluid or serum of patients. Prognosis depends on how quickly the disease is detected, identified, and properly treated.

**Methods:** Under our observation were 54 patients with different CNS autoimmune disorders. Used ELISA and Western blot for evaluation of paraneoplastic, ion (K and Na) channels AB. We studied mice brain slice immunofluorescence by anti-Hu, anti-Ma2, anti-NMDA, anti-voltage gated potassium channel-complex (VGKC-complex) and aquaporin 4. AB, neurological and somatic conditions of patients with autoimmune neurological pathology, brain MRI, EEG and EMG were performed.

**Results:** We found increased levels of Anti-Hu AB in patients with small-cell lung carcinoma. In experimental model in mice with inoculation by this tumor type mice demonstrated lethargic sleep in case of injection by Anti-Ma2 AB. Patients with this pathology demonstrated anxiety, memory loss, headache. Most symptoms were produced by anti-NMDAR AB. They include hyperactivity in open field, tremor, choreic hypekinesis, parasomnia. Immunohistochemistry demonstrated fluorescence of these AB in basal ganglia of affected mice. Animals with anti-aquaporin 4 AB showed early blindness. Neuromiotonia and seizures symptoms appeared in patients suffering from anti-VGKC-complex encephalitis caused by VGKC-complex AB, confirmed by EEG and EMG.

**Conclusions:** Combined autoimmune pathology study in patients and animals allows better understand of pathogenesis and identification of therapeutic strategies.
AN UNDERESTIMATED CAUSE OF BILATERAL VESTIBULOCHOCLEAR DISEASE.

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Background and Aims:: Autoimmune inner ear disease (AIED) is an uncommon but potentially treatable cause of progressive sensorineural hearing loss (SNHL). There is a lack of specific autoantibodies and obtaining tissue biopsy is impractical. We describe an uncommon etiology of progressive vestibulochoclear dysfunction.

Methods:: 61 years male presented with 3 months history of acute onset progressive bilateral SNHL with frequent episodic vertigo lasting 6-10 hours, with worsening on postural change. It was associated with vomiting, imbalance while walking. No history of fever, headache, earache/fullness, tinnitus. There were no features of diabetes mellitus or systemic autoimmune disease. Signs of vestibular dysfunction - bilateral horizontal & torsional nystagmus with abnormal dynamic visual acuity, Fukuda and head impulse tests. Otoscopy and ocular examination for keratitis or uveitis were normal.

Results:: Magnetic resonance imaging of brain and inner ear were normal. Computerized tomography of temporal bone with Poschls view was normal. Audiogram was suggestive of bilateral moderately-severe SNHL. Antinuclear antibody was positive (1:100). Systemic autoimmune diseases, Menieres disease, Sarcoidosis and Cogan’s syndrome were ruled out. Diagnosis of AIED was considered based on Garcia-Berrocal et al criteria. Patient was given methylprednisolone pulse therapy followed by oral prednisolone. His symptoms decreased significantly over 4 weeks and hearing threshold improved from 90 to 50. On one-year follow-up patient had no episodes of vertigo and his hearing threshold remained static.

Conclusions:: Due to lack of specific diagnostic tests, AIED should be considered in unexplained sub-acute progressive SNHL and vertigo with a low threshold for treatment with steroids. Response to treatment supports diagnosis and guides further immunotherapy.
Background and Aims:: Guillain-Barré syndrome (GBS) is a rare pathology causing acute flaccid paralysis with hypo- or areflexia. It is thought to mostly have a post-infective immunological-driven pathogenesis, as it is associated with bacterial and viral infections. Post surgical syndromes are described, although rare. Lumbar puncture is rarely complicated by iatrogenic infective myelitic or peripheral involvement, which could mimic GBS.

Methods:: A 55-year-old male in good health underwent spinal anesthesia for right achilles tendon rupture suture. Two weeks after recovery, he developed bilateral ascending radicular pain; at that time no deep tendon reflexes (DTR) abnormalities were noted. Upon inspection, hyperaemia, hyperthermia and swelling were evident at spinal anesthesia site. We performed an electrophysiological study, which turned unremarkable, and lumbar spine MRI, which showed an abscess posteriorly to L3-L4 spinous processes and cauda and leptomeningeal contrast enhancement. The patient remained apyretic during hospitalization and blood tests turned unremarkable. Laségue sign was positive bilaterally but no headache or meningismus were present. Moreover, performing a diagnostic lumbar puncture was deemed at high risk of CSF contamination. Patient’s DTR later disappeared, which prompted the beginning of IVIg therapy. An antibiotic course was also added for the subcutaneous lumbar abscess.

Results:: DTR reappeared and pain ameliorated after therapy; the patient was discharged with only mildly lowered tendon reflexes. On follow-up, MRI and EMG/ENG study turned unremarkable.

Conclusions:: Although not a typical complication, iatrogenic infective radiculitis could explain patient’s symptoms. In our case, anamnestic, clinical and instrumental features helped in excluding such diagnosis in favor of a GBS.
CEREBRAL AMYLOID ANGIOPATHY RELATED INFLAMMATION: STEROID RESPONSIVE OR SPONTANEOUSLY REMISSIVE BRAIN DYSFUNCTION?

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Background and Aims:: Definite diagnosis of cerebral amyloid angiopathy related inflammation (CAA-ri) requires histopathological features of vascular inflammation and amyloid deposition. However clinico-radiological criteria for CAA-ri have been recently introduced¹ and validated². Clinical syndrome shows dramatic improvement after immunotherapy³. However, spontaneous remission has been described in some patients⁴.

Methods:: We report seven patients with clinico-neuroradiological characteristics of CAA-ri. Clinical features at presentation included seizures, confusion, cognitive impairment and focal neurological signs. Diagnostic studies included infectious diseases and autoimmune work-up and brain MRI, as well as cerebral angiography and CSF analysis in two and one patients, respectively. Three patients were initially diagnosed as PRES or vasogenic edema secondary to vascular malformation.

Results:: Brain MRI showed prominent T2-weighted/FLAIR white matter changes associated with SWI/gradient-echo typical findings of CAA. All patients were diagnosed with CAA-ri. Three patients showed steroid-responsive brain dysfunctions; the remaining patients had a clinical and/or neuroradiological spontaneous remission. Three patients had been lost at follow-up.

A PROOF OF CONCEPT REPORT OF ASL MRI AND 18F-FDG PET IN LIMBIC ENCEPHALITIS

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Background and Aims:: Autoimmune limbic encephalitis (LE) is a condition characterized by seizures and cognitive dysfunction. Fluorine-18 Fluorodeoxyglucose (18F-FDG PET) has proved to be an important diagnostic and prognostic tool because it may detect brain metabolism in the earlier phases of the disease. Two main 18F-FDG PET patterns have been reported: a neurodegenerative one and a mixed hypermetabolic/hypometabolic. Arterial Spin Labelling (ASL) MRI reveals brain perfusion, that matches brain metabolism because they are strongly coupled. The aim of the present study was to evaluate patients with LE with both techniques.

Methods:: Two patients with LE underwent to 18F-FDG PET and ASL MRI scans. Areas of altered perfusion and metabolism were analyzed by visual inspection, and findings were compared between the two techniques.

Results:: One patient with LG1 encephalitis during a relapse performed 18F-FDG PET that showed an increased metabolism in the right hippocampus (mixed hypermetabolic/hypometabolic pattern). ASL MRI showed increased perfusion in the same area. One patient with seronegative LE underwent to 18F-FDG PET scan that highlighted left hemispheric hypoperfusion (neurodegenerative pattern). ASL MRI showed similar results.
Conclusions: ASL can detect the two main metabolic patterns described in 18F-FDG PET. This study provides a proof-of-concept that ASL technique could be implemented in the MRI protocols for LE, in order to provide a contrast- and radiation-free method to increase diagnostic performance and to evaluate disease activity even in the first MRI scan.
PARANEOPLASTIC NEUROMYELITIS OPTICA SPECTRUM DISORDER IN A PATIENT WITH BREAST CANCER AND ADIUVANT CHEMOTHERAPY

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Background and Aims: Neuromyelitis optica spectrum disorder (NMOSD), is an autoimmune inflammatory disorder of the central nervous system mostly associated with antibodies to AQP-4. It is generally idiopathic, but it is frequently associated with systemic autoimmune disorders and in some cases with neoplasm. We propose a case of NMOSD associated with breast cancer and potentially with its treatment.

Methods: A 50 years-old woman with a history of breast cancer and a recent cycle of adjuvant chemotherapy (Paclitaxel and Trastuzumab) was admitted to the Cardiology Department for pulmonary embolism and deep vein thrombosis. Subsequently she developed neurological features typical of a longitudinally extensive transverse myelitis. MRI was suggestive of NMOSD and antibodies against AQP-4 were detected in serum. Treatment with plasmapheresis was started, with a good outcome of the patient.

Results: Paraneoplastic NMOSD syndrome is a rare disease, sometimes associated with cancer. This condition is more typical in female patient aged over 50 years-old at symptoms onset and with breast cancer, and only few cases have already been described. We speculate that in our patient the disorder may have been not only caused by the cancer alone, but possibly by the chemotherapy too, considering the close timing relation with the treatment (few months). However, there are no cases in literature describing the link between NMOSD and Trastuzumab.

Conclusions: This case underlines that NMOSD may be an important complication of breast cancer and its therapies and prompt diagnosis may be imperative to achieve a better prognosis.
Background and Aims:: Background and aims: Autoimmune encephalitis are an upcoming group of immune mediated encephalitis, characterised by subacute onset neurological syndrome with supporting radiological and investigational evidence. The increasing awareness among clinicians, has led to spurt in the number of cases diagnosed. We present a series of autoimmune encephalitis with unusually long clinical history and syndromes.

Methods:: It was a prospective observational study from 2016-2019, it included all patients of antibody proven autoimmune encephalitis who had a prolonged clinical course and atypical clinical features. All of the patients had been misdiagnosed as psychiatric, neurodegenerative or cryptic disorders. The diagnosis was achieved with a combination of presence of serum antibodies, MRI, FDG PET and CSF findings.

Results:: A total of 4 cases of chronic form of autoimmune encephalitis were identified. The duration of symptoms varied between 1 year to 25 years. The corresponding MRIs didn't reveal significant changes of AIE, however FDG-PET of brain showed findings of hyper/hypometabolism and pointed towards the diagnosis of AIE.

Conclusions:: Chronic variants of AIE are difficult to diagnose. FDG PET of brain may help in identifying these cases earlier.
DELAYED SEROPOSITIVITY IN A PATIENT WITH ANTI-LGI1 LIMBIC ENCEPHALITIS

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Background and Aims:: Anti Leucine-Rich Glioma Inactivated 1 encephalitis (LGI1) is a rare autoimmune disorder caused by antibodies to synaptic voltage-gated potassium channels. Its typical manifestation includes seizures (mostly tonic-dystonic), hyponatremia, memory disturbances and behavioural changes. Patients may have temporal lobe abnormalities on EEG and brain MRI, instead CSF is often normal. In less than 10% of cases it is associated with cancer (commonly thymoma).

Methods:: A 54 years-old woman without any relevant medical history was admitted to our Neurology Department after subacute onset of moderate deficit on long term verbal memory, spatial disorientation and focal temporal seizures. Brain MRI and EEG showed respectively left hippocampal T2-weighted hyperintensity and left temporal epileptic discharges, both suggestive for limbic encephalitis. Extended laboratory and radiological examinations, including onconeural markers, antibodies against neuronal surface proteins and total body CT scan, were all negative.

Results:: Treatment consisted of glucocorticoids, IVIG and anti-epileptic drugs that brought to moderate improvement of cognitive status and EEG normalization. 20 months later the patient was reassessed and at that point the presence of antibodies anti-LGI1 on both blood and CSF samples was detected. Not any underlying neoplasm has been yet found.

Conclusions:: Although the most known features of anti-LGI1 encephalitis are dystonic seizures, our report suggests that its phenotype could be heterogeneous, including temporal seizures. Our experience suggests that the timing of seroconversion may be delayed, recommending subsequent reassessment of immunological status as well as tight radiological follow-up for possible hidden cancers.
RECURRENT ACUTE MOTOR AXONAL NEUROPATHY WITH COMPLETE RESOLUTION: A CASE REPORT

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**Background and Aims:** Inflammatory polyneuropathies, caused by direct autoimmunne attack on peripheral nerves can be classified as either acute (less than 4 weeks) and chronic (more than 4 weeks) or demyelinating and axonal. The commonest acute variety is demyelinating (AIDP) while the axonal varieties ‘acute motor axonal neuropathy’ (AMAN) or ‘acute motor and sensory axonal neuropathy’ (AMSAN) are responsible only for less than 5%. Acute inflammatory polyneuropathies are usually monophasic illnesses; although inflammatory demyelinating polyneuropathy (AIDP) or Miller-Fisher syndrome can recur. Recurrent AMAN are exceedingly rare. We report a case with two episodes on AMAN with complete resolution, occurring eight years apart.

**Methods:** A 36-year-old male presented with progressive weakness over 3 days involving all 4 limbs without involvement of sensory, autonomic nor cranial nerves. The respiratory muscles were involved requiring intubation and ventilation. He did not have any evidence of rheumatological, endocrine or autoimmune diseases. On examination he had a flaccid quadriparesis (power-0/5 MMRC) with global areflexia. The CSF protein was elevated without a cellular reaction and the nerve conduction studies were suggestive of AMAN. Except the newly diagnosed diabetes the rest of the haematological and biochemical investigations were normal.

**Results:** Eight years ago, he had developed a similar episode with nerve conduction evidence of AMAN which had completely resolved with IVIG (intravenous-immunoglobulins) and intense physiotherapy. He made an uneventful recovery in the current admission with the same treatment, but was not kept on long-term immunosuppressants.

**Conclusions:** Although exceptionally rare, the AMAN type of GBS can recur with prospects to recovery with immunotherapy and rehabilitation.
CENTRAL NEUROGENIC HYPERVENTILATION SECONDARY TO SERONEGATIVE AUTOIMMUNE ENCEPHALITIS

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\textbf{Background and Aims::} Central Neurogenic Hyperventilation (CNH) is a rare condition characterised by deep, rapid breathing. Diagnostic criteria for CNH include hyperventilation that persists during sleep, respiratory alkalosis with normal PaO$_2$ in the absence of drug or metabolic causes. Autoimmune encephalitis has varied clinical presentation. It poses a greater diagnostic challenge when there are no detectable antibodies in serum or CSF; these patients are classified as having seronegative autoimmune encephalitis.

\textbf{Methods::} Case Report

\textbf{Results::} A 74-year-old gentleman with a history of hypertension presented with subacute onset of gait unsteadiness which was gradually progressive for 2 months associated with recent-onset breathing discomfort. He also developed dysphagia to liquids>solids and odynophagia. Examination revealed cachexia, tachypnea (30-35/min), left upper and lower limb ataxia with gait unsteadiness, and a mild confusional state. CT Chest, Echo heart, and ECG were normal. MRI brain revealed a focal lesion in the left cerebellum, pons, and midbrain with patchy areas of diffusion restriction and contrast enhancement. Arterial blood gases were pH, 7.60; PaCO$_2$, 15mmHg; and PaO$_2$, 110mmHg. CSF analysis was normal and autoimmune autoantibodies were negative. On D9 of admission, he developed myoclonic jerks associated with worsening tachypnea. Electroencephalogram revealed generalized slowing and amplitude reduction. After ruling out infective and vasculitic etiology, seronegative autoimmune encephalitis was considered and pulse methylprednisolone was given for 5 days. There was a significant improvement in general sensorium and hyperventilation following steroid administration.

\textbf{Conclusions::} This article emphasizes the importance of diagnosing seronegative autoimmune encephalitis, which has a clinical profile and clinical outcome similar to seropositive AE but no diagnostic biomarker.
CHRONIC STEROID-DEPENDENT MYELITIS AND OPTIC NEURITIS: A CASE REPORT

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Background and Aims: A 34 year-old woman presented a subacute onset of right hemiparesis and right blurred vision. The head and spinal cord MRI revealed a longitudinally extensive transverse C5-D1 myelitis (LETM) and a posterior superior right optic nerve lesion, with peripheral irregular enhancement. No recent infections/systemic symptoms or other diseases were reported. General examination was normal. Neurological exam was characterized by moderate-to-severe ataxo-spastic gait, right weakness, left sensory loss and impaired vision in lower right eye field. Possible differential diagnosis were Neuromyelitis Optica and anti-MOG associated disorders, systemic autoimmune diseases, neurosarcoidosis and atypical paraneoplastic syndromes.

Methods: Diagnostic protocol: blood tests and CSF analysis, including microbiological and autoimmune exams, chest imaging and whole body 18-FDG-PET/CT.

Results: Blood, microbiological and autoimmune exams were normal. Serum was negative for anti-AQP4/MOG and paraneoplastic antibodies, as well as CSF, whose analysis revealed elevated proteins, normal IgG-index, oligoclonal bands type 4 and no cells. Chest imaging and whole body 18-FDG-PET/CT had no abnormalities, while Visual Evoked-Potentials showed right pre-chiasmatic disfunction.

Conclusions: Patient was treated with three cycle of high-dose intravenous corticosteroids but therapy discontinuation rapidly resulted in clinical and MRI disease reactivation, with extension of cervical lesions and persistent gadolinium-enhancement lasting more than three months. Intravenous immunoglobulin was not efficacious. Based-on clinical history and neuroimaging, both NMO and neurosarcoidosis were possible diagnosis, but the radiological characteristics and chronic steroid-dependence, led to possible neurosarcoidosis diagnosis. Full recovery was obtained after two months of continuous steroid treatment. Therefore, patient was shifted to methotrexate, with slow steroid tapering. Since then, no more clinical or radiological disease-activity occurred.
SARCOIDOSIS: CLINICAL AND PARACLINICAL FEATURES: A STUDY OF A TUNISIAN COHORT

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Background and Aims:: Sarcoidosis is characterized by its heterogeneous clinical presentation. The aim of this study is to describe clinical and paraclinical characteristics in a cohort of Tunisian patients with sarcoidosis.

Methods:: A retrospective study was conducted at the department of neurology and internal medicine of the Military Hospital of Tunis from 1997 to 2019. We included patients who were diagnosed with sarcoidosis. Clinical and paraclinical features were analyzed.

Results:: We included 65 patients with sarcoidosis. Mean age at presentation was 46.68 years. Neurological symptoms were the first clinical manifestation of sarcoidosis in 14% of cases. The most common manifestations included central nervous involvement and cranial neuropathies. Pulmonary sarcoidosis is observed in 47 patients and ophthalmological involvement is present in 26 patients. Magnetic resonance imaging (MRI) showed a variety of manifestations including diffuse intraparenchymal inflammatory lesions in the brain and spinal cord, leptomeningeal enhancement and optic nerve involvement. Pleiocytosis and elevated CSF protein were found in 14 patient. The genetic study concerned only 50 patients. A high frequency was found for the HLA DRB1 * 1501 , HLA-DRB1 * 0301 and the D allele for the angiotensin-converting enzyme gene. First line therapy with corticosteroids was initiated in 56 cases. Second line therapy consisting of azathioprine and hydroxychloroquine was initiated in 12 cases. Outcome consisted of complete remission in 17 patients.

Conclusions:: Diagnosis of sarcoidosis is difficult due to its clinical polymorphism. Recent advances in the pathophysiology and genetics could have therapeutic implications for early management of these patients.
Background and Aims:: N-methyl-D-aspartate receptor (NMDAR) encephalitis is a potentially treatable condition, although a small proportion of patients remains refractory to immunotherapy. Recently, bortezomib, a proteasome inhibitor used in multiple myeloma, has been used in NMDAR encephalitis and neuromyelitis optica. We performed a systematic review regarding the use of bortezomib in NMDAR encephalitis

Methods:: We performed an independent PubMed search employing “Anti-N-Methyl-d-Aspartate encephalitis AND bortezomib”, including papers published between January 1st, 2007 to June 30th, 2020. Clinical and demographic data were collected. We compared paraneoplastic and non-paraneoplastic encephalitis and patients with favorable (modified Rankin Scale (mRS) ≤2) and unfavorable outcome. Fisher and U-Mann Withney tests were used as appropriate (p-value<0.05).

Results:: Twelve articles were included, with 21 patients. The quality of studies was overall poor. Median age at onset was 26 (8-61) and 7 patients (33.3%) had paraneoplastic encephalitis. Median number of previous treatments was 4 (3-7). 10 patients (47.6%) had a favorable outcome after bortezomib and 9 (42.9%) patients developed side effects. Patients with paraneoplastic encephalitis underwent more frequently to oophorectomy (p=0.010). Patients with favorable outcome were younger (p=0.043) and had lower cerebrospinal fluid NMDAR antibody titer at onset (p=0.006), underwent more frequently to anti-epileptic drug reduction (p=0.035) and had fewer side effects (p=0.044).

Conclusions:: Nearly half of patients with NMDAR encephalitis treated with bortezomib improved, however about half of treated patients developed side effects. The overall quality of published evidence is low and further studies should be performed with systematically defined endpoints and in larger and homogeneous cohorts.
NEUROMYELITIS OPTICA SPECTRUM DISORDERS (NMOSD), SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND MG RESULTS IN TRANSVERSE MYELITIS

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Background and Aims:: Considering the rarity of such a combination of nosologies, we present this clinical case.

Methods:: A 51-year-old female patient was admitted to the neurology department with complaints of a weakness in the lower limbs; periodic leg pain; feeling of constriction in the ribs area “like a belt”; urinary incontinence. These symptoms bothered her for 1 year, with alternating exacerbations and improvements. A history of MG since 1997. During the study medical history, somatic and neurological status, laboratory, neuroimaging data were evaluated.

Results:: In neurological status: lower spastic paraparesis, superficial sensitivity was impaired in a mosaic pattern, paresthesias in both legs. Pelvic functions - incomplete emptying/incontinence. No ophthalmologic pathology. Laboratory: CRP - 1.02 mg/l (<6.00), RF <20.00 IU/ml (<30.00); antiDNA: 67.30> U/ml (<25), ANZA 1:10 (<1:10), atypical type of fluorescence; positive analysis for ANF, homogeneous (1: 1000) and granular types of fluorescence (1: 320). ANA screening, immunoblot were negative; complement C4 - 0.14 g/l (0.15-0.57). AQP4-IgG titer 1: 320 (<1:10). Thoracic spine MRI with contrast: Th2-Th5 – increased MR-signal in T2 mode; no contrast accumulation. Based on 4 SLICC criteria (ANF, antiDNA, reduced complement fraction, CNS damage) SLE was diagnosed. Considering the anamnesis, clinical, laboratory, MRI data, autoimmune myelitis was diagnosed, stage of exacerbation. Courses of infusion pulse therapy with methylprednisolone, high-volume plasma exchange №5, therapy with cyclophosphamide and rituximab (1000 mg/2 week №2) were completed, with good clinical improvement. Patient monitoring will be continued.

Conclusions:: NMOSD in combination with SLE and MG is a rare situation and causes significant diagnostic difficulties.
ANTI-SMOOTH MUSCLE ANTIBODIES (ASMA) AND VERBAL DYSCALCULIA. A NEW TYPE OF AUTOIMMUNE ENCEPHALITIS.

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Background and Aims:: F-Actin is ASMA’s molecular target; it forms microfilaments and actin patches. ASMA could lead to dendritic spines retraction causing cortex reduction and cognitive impairment as described in chronic ASMA patients. We have identified a new type of AE due to ASMA, neither reported or classified up to date. The aim is to describe a new type of Autoimmune Encephalitis (AE) due to ASMA, whose core clinical presentation is verbal dyscalculia.

Methods:: We present a series of seven patients diagnosed with encephalitis due to positive ASMA presenting with somnolence, changes in personality and mentation with amnesia, bradypsychia, inattention, dysthymia, asthenia, adynia, and dysesthesia. Physical examination showed verbal dyscalculia as the most common and earliest clinical sign, followed by decreased cognition, Romberg’s, Hoffman’s, Babinski’s, frontal releases signs, altered DTRs, hyperekplexia, dystonia, tremor, aphasia and involuntary movements on extremities. Blood work showed positive ASMA and elevated CRP. Two patients showed mildly elevated LFT. Only one had F-actin measured with positive results. None of the patients showed signs of cirrhosis. Patients had abnormal EEGs with generalized slow waves and MRI had discrete insular and parieto-occipital cortical hyperintensities.

Results:: Patients showed improvement after being treated with Methylprednisolone and Rituximab.

Conclusions:: We propose a new type of AE due to ASMA, with verbal dyscalculia as the most common and earliest clinical sign which is accompanied by personality, neurophysiological and serological changes without hepatic disease manifestations (commonly referred by us as Trillo’s encephalitis). We believe that cortex reduction and cognitive impairment could be explained by ASMA relationship with F-actin.
ANTI-GAD AUTOIMMUNE ENCEPHALITIS RESEMBLING LONG TERM CHRONIC DISOCIATIVE AMNESIA CASE REPORT

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Background and Aims: GABA plays a major role in the formation of memory in insula, prefrontal cortex, and hippocampus. Neuroinflammation induced by GABA dysregulation and GABAr signaling changes leads to an overall GABA deficit. These cell-mediated inflammatory changes have been associated with motor symptoms, short term anterograde amnesia and neuropsychiatric features such as hallucinations. The aim is to report a case of Anti-GAD AE with organic memory loss resembling long term chronic dissociative amnesic disorder lasting over 15 years.

Methods: A 58 years old Hispanic male with a history of 20 years of disease triggered by a stressful event, followed by 15 years of global amnesia with fugue like symptoms that suddenly ended after a religious delusion. He complained of bilateral periorbital pain, loss of consciousness with drop attacks and involuntary movements while sleeping, nightmares, mood disturbances towards depression, anxiety, religious hallucinations, and fatigue. At examination he was hypertensive, with tangential speech, personality changes, neck stiffness, limb rigidity with positive trigger points and right hemiparesis, Bilateral Hoffman’s, hyperreflexia, involuntary movements, tremor, Romberg’s, and impaired memory with positive frontal release signs. Blood work showed abnormal Anti-GAD, elevated CRP, ESR, creatinine and elevated proteins in CSF 86. MRI found multiple bilateral lacunar infarcts. EEG showed right temporocipital disorganization and generalized slow waves.

Results: The patient was treated with IV methylprednisolone, oral prednisone, paroxetine, baclofen, clonazepam and levetiracetam with clinical improvement.

Conclusions: To our knowledge this is the longest time of organic memory loss symptoms resembling long term chronic dissociative amnesia reported due to Anti-GAD AE.
EPISODIC ATAXIA AS A PRESENTING SYMPTOM OF ANTI-NMDAR ENCEPHALITIS

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Background and Aims:: Anti-NMDA receptor (anti-NMDAR) encephalitis presents commonly with cognitive and psychiatric symptoms, but also movement disorders are reported. Cerebellar ataxia has been described in young children, but it is uncommon in adults. Among paroxysmal movement disorders, dyskinesias are reported. Episodic ataxia is extremely rare and never reported as a presenting symptom.

Methods:: A 61 years-old woman came to our attention for sudden onset of ataxia and confusion while she was at a dinner (she had begun compulsively eating and drinking alcohol). Brain CT, CT angiography, and CT perfusion were negative. The alcohol test was positive and blood examination revealed mild hyponatremia. A diagnosis of pancerebellar syndrome due to alcohol intoxication was made. After hydration, the patient presented a complete regression of symptoms. After one year she returned for an episode of acute confision that occurred on her way to work. The alcohol test was negative, and EEG was unrevealing. The neurologic examination showed confusion, marked bilateral ataxia, and dysarthria, with subsequent complete regression after 12 hours. In the previous 10 months weight loss, depressive symptoms, and working memory deficits were reported, and her husband referred she has become more irritable and talkative than usual.

Results:: MRI scan showed mild cerebellar atrophy. Laboratory tests revealed hyponatremia (Na: 130 mmol/L). CFS examination was within the limits, while blood autoimmune panel revealed a positivity for Ab anti NMDAR, supporting the diagnosis of anti-NMDAR encephalitis.

Conclusions:: Despite the rarity of this phenomenon, episodic ataxia can be a presenting symptom of anti-NMDAR encephalitis.
FETAL OUTCOME IN ANTI-NMDAR ENCEPHALITIS DURING PREGNANCY: A SYSTEMATIC REVIEW.

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Background and Aims:: Anti-NMDA receptor encephalitis is an autoimmune inflammatory disease which mainly affects young women, causing psychiatric and neurological manifestations. Pathogenic antibodies target extracellular domain GluN1 subunit receptor. An increasing number of reports show that anti-NMDAR encephalitis can occur also during pregnancy leading to maternal and fetal distress. In this systematic review we analyzed fetal outcome after maternal anti-NMDAR antibodies exposure during pregnancy, summarizing the available data.

Methods:: We performed a systematic review according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Epidemiological, clinical, laboratory and neuroimaging data of pregnant women with anti-NMDAR encephalitis and their newborns were collected. Outcomes of the infants were based on clinical features, developmental abnormality, atypical behavior, APGAR score and neuroimaging.

Results:: A total of 20 articles (37 cases) were included. The incidence of anti-NMDAR encephalitis was higher during the first trimester of pregnancy. Ovarian teratoma was found in 2/37 cases. Immunotherapy was used in 20% of cases. Pregnancy outcome was positive in 80% of cases with less than 10% of newborns suffering from transient neurological or respiratory symptoms. Prematurity was found in 40% of cases. At the follow-up, children’s neurocognitive development impairment was found in less than 20% of patients. Data actually showed transplacental antibodies transition. Infants with neuropsychiatric symptoms often had anti-NMDAR antibodies serum positivity.

Conclusions:: Anti-NMDAR encephalitis can be a severe comorbidity during pregnancy. Pregnancy and fetal outcome is usually positive, though children neurocognitive development impairment can occur. Long-term effects of fetus anti-NMDAR antibodies exposure have to be better explored.
OUR CLINICAL EXPERIENCE IN THE TREATMENT OF MYASTHENIA GRAVIS ACUTE EXACERBATIONS WITH A NOVEL NANOMEMBRANE-BASED THERAPEUTIC PLASMA EXCHANGE TECHNOLOGY

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Background and Aims:: The intravenous immunoglobulins (IVIG) and therapeutic plasma exchange (TPE) are equally effective rapid-acting immunotherapies in myasthenia gravis (MG) acute exacerbations. However, according to the American Academy of Neurology 2011 plasmapheresis guideline there is insufficient evidence to support or refute the use of plasmapheresis for MG, which clinical relevance is the aim of our study.

Methods:: 36 adult patients, MGFA 4/4B and 5, with 45 acute MG episodes were entered into a before-after study to compare the standard treatment (before group, n=24) with advanced one using a novel nanomembrane-based TPE (after group, n=12). All patients were treated by a team of neurologists and anestesiologists/intensivists in an academic NeuroICU according to the local guidelines. TPE or IVIG infusions were used in impending and manifest myasthenic crisis (MC), or selectively in patients at high risk for prolonged intubation. The clinical improvement was checked on forms filled in routinely upon admission and on transfer from the ICU using Myasthenia Muscle Score (0-100), with at least 20 points increase for responders. Data regarding immunoglobulin levels, noninvasive ventilation (NIV), invasive mechanical ventilation (IMV), tracheotomy, duration of IMV, ICU and hospital stay, TPE and IVIG consumption, and overall mortality were collected as well.

Results:: There were no between-group changes in survival and IVIG consumption, but a remarkable increase in the use of TPE (71%) and NIV trial (58%), and a reduction of early tracheotomy with 1/2 after the introduction on nanomembrane-based TPE.

Conclusions:: The novel TPE technology shifted our clinical practice towards more preventive rather than protective MC complications treatment.
DIAGNOSTIC DILEMMA IN SUSAC SYNDROME

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**Background and Aims:** Susac syndrome is an autoimmune endotheliopathy which specifically affect brain, retina and inner ear. The condition is common in young females (20 - 40 years). The diagnosis is made by presence of encephalopathy, branch retinal artery occlusion and sensory neural hearing impairment. Typical reversible “snow ball” appearance in the central corpus callosum favors the diagnosis. Condition could be successfully treated with IV steroids and Immunoglobulin if identified early.

**Methods:** Case She was a 32-year-old diagnosed patient with tension headache and idiopathic epilepsy, for one year. Ten months ago she had been treated with Aspirin for right branch retinal artery occlusion. Six months later she had felt worsening of right vision, leading to the diagnosis of Optic neuritis and was treated with oral Prednisolone, resulting mild improvement. Two months back, she presented with left side visual and Bilateral hearing impairment. There was a peripheral scotoma on visual perimetry and Pure tone audiometry showed sensory neural hearing impairment. At current presentation, her left vision had improved completely following IV Methyl Prednisolone, but there was right optic atrophy and VEP showed delayed P100. MRI done 6 weeks later showed no significant abnormality.

**Results:** The clinical history and response to steroids led to make the diagnosis of Susac syndrome. Previous delay in diagnosis due to incomplete clinical presentation had left some permanent disabilities on the patient.

**Conclusions:** The presentation of Susac syndrome could be nonspecific. Early identification and prompt treatment warrant good recovery. Therefore, the knowledge of this rare condition among health care professionals is important.
AN AMBISPECTIVE COHORT STUDY OF CHRONIC INFLAMMATORY DEMYELINATING NEUROPATHY, AND ITS VARIANTS

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Background and Aims:: BACKGROUND : The clinical presentation, findings, and outcome may vary between typical chronic inflammatory demyelinating polyradiculopathy (CIDP) and its variants. Aims and Objective: To compare clinical profile and outcome of typical CIDP and its variants.

Methods:: Setting: Tertiary care referral hospital. Materials and Methods: The CIDP patients diagnosed as per EFNS/PNS criteria were included. Hospital records were assessed to note retrospective data of patients included. Prospective patients were subjected to detailed history and examinations. The clinical disability was assessed using ODSS, NIS, IRODS, SCOPA AUT scales. Based on presentation and investigations for underlying diseases, the patients were categorized into typical CIDP and its variants. Treatment prescribed was noted and outcome was assessed at 3 months. The study is ongoing and intends to recruit 100 patients.

Results:: A total of 34 patients have been included till now, ranging from age 20 to 76. 10 (29.4%) had atypical CIDP, POEMS being the commonest variant (7), followed by MADSAM (2) and diabetic amyotrophy (1). Age and sex distribution was similar in both groups, however atypical CIDP had worse scores on ODSS, NIS, IRODS and SCOPA scales, had more relapses (30% vs 0 %) and required polytherapy (90% vs 62.5 %) compared to typical CIDP. The study intends to assess treatment response in both groups after 3 months.

Conclusions:: Of the total patients with CIDP, 29.4% of patients had atypical CIDP which was associated with more severe presentation, more relapses and less response to treatment, requiring the use of polytherapy.
OCRELIZUMAB MODIFIES CIRCULATING IMMUNE ASSET IN RELAPSING-REMITTING MULTIPLE SCLEROSIS SUBJECTS.

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Background and Aims:: Multiple Sclerosis (MS) is a chronic autoimmune disease of the central nervous system, mediated by autoreactive lymphocytes. Ocrelizumab, a humanized monoclonal anti-CD20 antibody, has shown pronounced effects in reduction of disease activity. Although the clinical response to Ocrelizumab is related to a specific B cell depletion, other circulating lymphocytes may be affected by this treatment.¹ Here, we investigated overtime the possible effects of Ocrelizumab on circulating immune asset in relapsing remitting (RR)-MS subjects.

Methods:: In this prospective longitudinal study, we enrolled n=20 treatment-naïve RRMS patients and n=20 age-sex-BMI-matched healthy controls. RRMS patients were treated with Ocrelizumab and followed up for 6 months. Frequency and phenotype of several circulating immune T cell subset were evaluated by flow cytometry.

Results:: Before initiating treatment, RRMS patients showed lower percentage of lymphocytes compared to healthy subjects. In particular, lower frequency of naïve T cells was observed (i.e., CD4⁺CD45RA⁺ and CD8⁺CD45RA⁺ cells). On the contrary, RRMS patients had higher frequency of both memory T lymphocytes (i.e., CD4⁺CD45RO⁺ and CD8⁺CD45RO⁺ cells) and activated T cells, revealed by HLA-DR expression marker. Six months after the treatment, further reduction of lymphocytes was observed, due to the B cell loss. However, we noticed increased frequency of T cell subset with naïve phenotype. In parallel, a reduction in the activated/memory T cells was observed.

Conclusions:: Together these findings suggest that Ocrelizumab influences also T cell compartment, favoring reduction of activated/memory T cells in RRMS patients.
APPLICATION OF THE APE2 AND RITE2 SCORES IN PATIENTS PRESENTING WITH COGNITIVE DYSFUNCTION

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Background and Aims:: To assess the performance of the Antibody Prevalence in Epilepsy (APE2) and Response to ImmunoTherapy in Epilepsy (RITE2) scores in patients with cognitive dysfunction of unknown etiology.

Methods:: We prospectively collected clinical and paraclinical data of 58 patients referred to our Neurology Unit between January 2020 and December 2020 for altered consciousness level, short term memory loss, or cognitive/neuropsychiatric dysfunction of unknown aetiology. Cell-based assays, tissue-based assays, immunoblot, were performed in serum/cerebrospinal fluid to detect neuronal/glial antibodies. The APE2 and RITE2 scores were calculated and compared with clinical and laboratory data.

Results:: Antibodies were detected in 13/58 patients (22.8%). The APE2 score was significantly higher in patients with antibody positivity (median 6, range 2-11) compared with antibody negative cases (median 4, range 1-9) (P=0.038 Mann-Whitney). An APE2 score>=4 showed a sensitivity of 61.5% and specificity of 40% for the presence of neuronal antibodies and a sensitivity of 78.5% with a specificity of 45.4% for criteria-confirmed diagnosis of autoimmune encephalitis. Using a cut-off of>=5, we increased the sensitivity to 69.2% and the specificity to 68.1% for the presence of neuronal antibodies. Overall, 25 patients received immunotherapy. A RITE2 score>=7 showed a sensitivity of 71.4% and a specificity of 45.4% in predicting a good clinical outcome (improvement in mRS>=1).

Conclusions:: This is the first attempt to independently validate the APE2 and RITE2 score in patients with cognitive impairment. Although useful, both scores performed less well than previously reported. A larger cohort is needed to confirm this result.
EFFICACY AND SAFETY OF RITUXIMAB THERAPY IN PATIENTS WITH AUTOIMMUNE NEUROLOGICAL DISORDERS

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Background and Aims:: Our aim was to examine the efficacy and safety of rituximab, an anti CD20 monoclonal antibody targeting B-cells, in patients with autoimmune neurological disorders (AND).

Methods:: We retrospectively assessed the incidence of adverse events (AE) and serious AE (SAE) in AND patients who received one or more continuous cycles of rituximab infusions. An extensive screening for infectious disorders, including hepatitis B (HBV) and C virus (HCV), HIV, tuberculosis, and Strongyloides stercoralis (SS) infection was performed before starting the therapy and every 6-12 months. Patients were clinically evaluated about every 3 months.

Results:: We included 19 patients who received rituximab for AND, including autoimmune encephalitis (n=5), neuromyelitis optica spectrum disorder (n=4), stiff person syndrome (n=2), myasthenia (n=4), inflammatory neuropathy or myopathy (n=3) and vasculitis (n=1). Four patients had a positive infectious screening (2 HBV positive, 1 HCV, 1 quantiferon positive and 1 SS positive). All patients with an infectious disorder received appropriate specific therapy before and over the whole course of rituximab therapy. There were a total of 1 AE and 1 SAE with rituximab treatment, both observed after a single infusion. No disease activity was detected in patients with infectious disorders. Improvement or stabilization of the AND was observed in 13/17 patients who completed at least one cycle.

Conclusions:: This study demonstrates that of peripheral B-cells appears safe and efficacious in treating AND when an accurate infectious screening and appropriate treatment are performed. Longer and larger prospective studies are needed to ascertain risks associated with chronic B-cell depletion.
NEUROLOGIC COMPLICATIONS OF CROHN'S DISEASE

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Background and Aims:: Crohn’s disease (CD) is frequently accompanied by systemic complications, but neurologic involvement is uncommon and only few cases are reported in the literature. We report three cases of CD with neurological complications occurring during episodes of increased disease activity.

Methods:: We conducted a search in the medical registry of our department to identify patients with CD and neurological complications. Three medical charts were found and retrospectively reviewed.

Results:: Mean age at neurologic manifestations onset was 45 years. Male to female ratio was 2/1. Neurologic involvement reveals the disease in two cases. The first patient, a 58 years old man, developed an acute motor sensory axonal polyradiculoneuritis while two patients had central nervous system involvement (seizures revealing superior sagittal sinus thrombosis with hemorrhagic infarct in one case and multiple subcortical small infarcts on brain MRI in the other case). The outcome was fatal for two patients; while a progressive improvement was observed in the last case.

Conclusions:: The association of neurological disorders with CD is well established. CD is complicated by an increased frequency of arterial and venous cerebrovascular disease as a consequence of probable hypercoagulability. Mixed sensori-motor axonal neuropathy was also described. Pathogenesis of peripheral involvement seems to be multifactorial including an autoimmune phenomenon affecting the small vessels of peripheral nerves. Folate deficiency has been proposed as an etiological factor in some cases. Gastroenterologist must be aware about neurological complications of CD and its screening should be performed systematically in order to avoid fatal outcome and neurological deficit.
EXPOSURE TO FARM ANIMALS AND MULTIPLE SCLEROSIS: WHAT'S THE RELATIONSHIP?

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**Background and Aims::** Multiple Sclerosis (MS) is a complex disease of the central nervous system, and aetiological factors continue to be uncovered. Inconsistent evidence exists regarding the association between exposure to pets and/or other animals and MS risk. We aimed to demonstrate the role of animal exposure's and MS development.

**Methods::** Population based case-control study was conducted in the neurological department of Habib Bourguiba Hospital. Patients with clinically definite MS cases and controls randomly chosen from the community were matched on sex and age. Data was collected from questionnaire detailing pet/animal exposure over the course of participant's lives.

**Results::** 30 patients and 30 controls were included in our study. Animal exposure was noted in 70% of patients with MS versus 37% of healthy controls. Exposure to farming, livestock and specific farm animals showed a significant association with MS risk (p=0.02). Exposure to sheep prior to disease onset was associated with a greater risk of MS (p=0.01) with Odds ratio=0.44 (0.7-0.27). No significant relationship was found between exposure to cats, dogs and rabbits and MS.

**Conclusions::** according to literature data, exposure to farm animals and especially sheep can leads to development of MS. This finding may be explained by the role of Clostridium perfringens epsilon toxin (ETX), wich is bacteria is most commonly linked to a gut infection in sheep, may be a blood-borne trigger for forming MS lesions based on its tropism for blood-brain barrier vasculature and CNS myelin.
COGNITIVE FUNCTION RECOVERY IN PATIENT WITH SEVERE ANTI-N-METHYL-D-ASPARTATE RECEPTOR (ANTI-NMDAR) ENCEPHALITIS

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Background and Aims:: Background Cognitive function impairment is one of the most major symptoms of Anti N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis. This phenomenon can be explained since Anti-NMDAR encephalitis occurs diffusely, affecting NMDA receptors that regulate synaptic transmission. Although improvement may be seen in approximately 80% patients who receive early immunotherapy, about 75% of patients still suffers from cognitive deficits. Aims To report a recovery of cognitive function in a case of severe anti-NMDAR encephalitis.

Methods:: Case A 26-year-old otherwise previously healthy woman was admitted with complaint of localized seizure. Despite initial improvement with medication, her condition deteriorated further with additional symptoms of behavioral changes, cognitive decline, visual hallucinations and new onset refractory status epilepticus (NORSE) that failed to respond with combination of three anti-epileptic agents. She was then transferred to ICU and diagnosed with anti-NMDAR encephalitis after further investigations were conducted. She underwent plasmapheresis and regained consciousness with improvement in her symptoms. However, she still suffered cognitive deficits especially in memory, attention, language, executive function and self-care with MMSE score of 15 and MoCA of 8 one month after discharge (Fig. 1). These deficits impaired her daily function despite no other symptoms.

Results:: Result On one-year follow-up after extensive rehabilitation, she reported significant improvement in self-care, attention, language, and executive function with slight deficit left in short term memory with MMSE score of 30 and MoCA of 26. She had since resume her work and life normally.

Conclusions:: Conclusion Early treatment and rehabilitation play a pivotal role for cognitive function improvement in anti-NMDAR patient.
Background and Aims:: Autoimmune encephalitis (AE) is a complex disorder, whose phenotypic spectrum has not been thoroughly defined. The main features (i.e. memory impairment, psychiatric manifestations, seizures) suggest the prominent involvement of the limbic system. Considering its close anatomo-functional correlations with the central structures subserving smell, we investigated olfaction in a population of AE patients.

Methods:: Adult subjects followed diagnosed with AE and followed for ≥ 6 months were enrolled. The Brief Smell Identification Test (B-SIT), a 12-item, forced-choice, scratch-and-sniff measurement was administered. According to B-SIT score, patients were classified as anosmic (<6), hyposmic (<9) and normal (≥9). All participants underwent anterior rhinoscopy to exclude major nasal conditions. Electro-clinical, laboratory, neuroimaging data were reviewed.

Results:: Nineteen subjects (14 males, median age 64 years) with definite (14/19) or probable/possible (5/19) AE were included. Smell impairment was revealed in 15/19 patients (78.9%), 9 hyposmic and 6 anosmic. Age, gender and smoking habit did not affect B-SIT. Olfactory dysfunction appeared more common among patients with definite AE (p=0.0374), regardless of autoantibody status. Participants with higher modified Rankin Scale (mRS) scores at AE onset more often had hyposmia/anosmia (p=0.027). Subjects with bilateral EEG abnormalities were more likely to present smell impairment (p=0.006).

Conclusions:: We found olfaction to be impaired in a large proportion of AE patients, independent of autoantibody status. Olfactory dysfunction appeared more common in subjects with severe AE (as indicated by both definite diagnosis and higher mRS score), and might represent an additional feature suggesting the immune-mediated etiology of encephalitis.
Background and Aims:: Churg-Strauss syndrome (CSS) is a rare small and medium vessel necrotizing vasculitis. Peripheral nervous system involvement in CSS is extremely common, usually manifesting as mononeuritis multiplex or symmetrical peripheral neuropathy with typically a chronic onset. Central nervous system (CNS) involvement is quite rare, ischemic lesions are the most frequent CNS manifestations while cerebral hemorrhages are extremely uncommon.

Methods:: Herein, we report a case of a 55-year-old woman with atypical clinical presentation of CSS.

Results:: The patient was admitted to the hospital with distal weakness, mild hypoesthesia and pain of the lower limbs. She reported an acute onset of symptoms at about 3 days before admission to the hospital. The patient’s past medical history was significant for allergic rhinitis, sinusitis and one episode of asthmatic attack. The diagnostic examinations showed a severe acute distal axonal polyneuropathy and intracerebral hemorrhage with signs of a previous subcortical microhemorrhage. Laboratory tests revealed new HCV infection, without cryoglobulinemia and normal complement levels. CT scan of the chest showed diffuse pulmonary interstitial thickening with multiple ground glass opacity areas. Basing on the presence of 5/6 of major criteria the patient was diagnosed with CSS. Treatment with intravenous immunoglobulin followed by oral prednisone was started, leading to clinical improvement.

Conclusions:: In conclusion, physicians should be aware that intracerebral hemorrhage can be a rare presenting feature of CSS vasculitis. Furthermore, it would be valuable study if a new HCV infection could predispose to atypical onset with acute polyneuropathy or CNS involvement.
Background and Aims: Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) – is a recently designated inflammatory central nervous system (CNS) disorder, prominently involving the brain and in particular the pons. Etiology of the disease is unknown. Discussions are underway on whether this is an isolated disease or a syndrome that characterizes a number of other diseases. This pathology was first described by Pittock et al. in 2010. Currently in the world there are about 50 patients with this syndrome. We report the following patient with typical symptoms that are consistent with CLIPPERS syndrome.

Methods: We used the general clinical method, MRI and other additional examinations to determine this disease.

Results: CLIPPERS is a newly diagnosed disease, which was first talked about in 2010. His etiology is still unknown and the pathogenesis of this syndrome is not fully understood. It is not clear whether this is an isolated disease or a group of such illnesses. To determine the criteria for setting this diagnosis, you need more information about this syndrome. Therefore, it's important to publish new cases of CLIPPERS.

Conclusions: Characteristic features of CLIPPERS are mainly the lesion of the bridge, hence the clinical picture, a characteristic MRI picture and a good reaction to glucocorticoids. At this stage, this pathology is an exclusion syndrome. In our case, there are all indications that may indicate the CLIPPERS syndrome, especially since we have excluded a number of diseases that run on similar signs.
GLUR3 ENCEPHALITIS WITH COGNITIVE IMPAIRMENT, ATAXIA AND DYSKENESIA: TWO CASE REPORTS

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Background and Aims:: GluR3 antibodies are observed in patients with seizure and Rasmussen’s encephalitis. We report GluR3 antibodies positivity in two patients with subacute onset of movement disorders and ataxia.

Methods:: A 67-year-old male patient was referred to our Institution for a generalized weakness associated with hypophonia. Neurological evaluation showed a marked lower limb ataxia, generalized dyskenesias, decomposition of saccades, tongue motor impersistence and psychiatric symptom such as apathy, mental confusion and altered mood. Brain MRI did not reveal any lesion, EEG was normal, CSF assays, including prion protein, were negative. Serum onconeural antibodies were undetectable. Search for associated tumors was negative. A CNS surface antigens assay showed a presence of GluR3 antibodies in serum and CSF samples. Patient was treated with intravenous immunoglobulins (IVIg) and steroids with a complete remission of symptoms. A 56-year-old female patient was referred to our Institution for generalized seizure associated with motor impairment. Neurological evaluation showed a lower limb ataxia, dyskenesia and cognitive impairment. Brain MRI was unspecific. EEG showed epileptic alterations responsive to carbamazepine. Prion protein in CSF and serum onconeural antibodies were undetectable, whereas CNS surface antigens assay showed GluR3 antibodies in serum and in CSF samples. A course of IVIg led to a marked improvement in EEG alterations and ataxia, with movement disorders resolution.

Results:: These cases show that GluR3 antibodies may be not only related to seizure spectrum, but also to cognitive impairment and movement disorders.

Conclusions:: As GluR3 antibodies mechanism of action is still unclear, further studies are required.
ABNORMAL PRESENTATION AND IMAGING FINDING OF ANTI-NMDA RECEPTOR ENCEPHALITIS, A REPORT OF TWO CASES.

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Background and Aims:: Meningitis and myelitis are a very rare atypical presenting feature of anti-NMDA receptor encephalitis. We describe an unusual clinical presentation of anti-NMDA receptor encephalitis, the first case with a typical picture of meningitis followed by encephalitis, the second case with myelitis followed by psychiatric prodroma. We aim to widen the differential diagnosis in two patients presenting with clinical meningitis and myelitis followed by other common clinical symptoms and signs.

Methods:: The first case of a 17-year old woman who initially presented with a lymphocytic meningitis attributed to a viral infection. She subsequently developed fluctuating consciousness, agitation, visual hallucinations, dyskinetic movements. The second case of a 19-year old woman who presented with numbness and paresthesia attributed to cervical myelitis. She subsequently developed anxiety, insomnia, agitation, visual hallucinations, and autonomic instability.

Results:: Investigations in both patients revealed a diagnosis of anti-NMDA receptor encephalitis, with a high titer of antibodies in both serum and CSF. Neuroradiology evaluation of the first case showed typical pachymeningitis with contrast enhancement (Figure 1, A) while the second case showed a posterior cervical cord lesion (Figure 1, B). Both patients made an excellent recovery with immunotherapy, plus removal of an ovarian teratoma in the first case.

Conclusions:: Clinicians should consider autoimmune encephalitis in individuals with meningitis, particularly where extensive investigations fail to identify a causative pathogen and there is a rapid development of an encephalitic phenotype as first case. Moreover, acute myelitis accompanied by severe psychiatric manifestations should expand differential diagnosis to autoimmune encephalitis as a possible cause as the second case.
Background and Aims: Thymectomy plays an important role in producing a durable improvement of symptoms, reduction of medication requirement, and even medication-free remission in most of myasthenia gravis (MG) patients. However, variables potentially affecting remission have not been analyzed. Our aim was to compare the post-thymectomy prognosis in different conditions of MG patients with thymus pathologies.

Methods: We retrospectively analyzed MG patients who was referred to Neurology Department, Sahloul university hospital, Sousse, Tunisia and had undergone a thymectomy between 2015 and 2020. Dividing into different groups was based on gender, age of onset, duration of disease, thymus abnormalities and acetylcholine receptors (AChR) antibodies status to analyze different prognosis in different groups after one year post-thymectomy.

Results: Thirty-five patients were included. Complete stable remission (CSR) was achieved in 18 of 35 patients (51.4%). There is no gender neither antibodies status-related difference in achieving CSR. Patients with early onset of MG (=<50 yearsold) or disease duration less than 12 months had higher CSR rates without significant association (p=0.09 and p=0.25 respectively). While no difference was found in remission rate between thymus pathologies (p=0.56).

Conclusions: Early onset myasthenia gravis patients who had early thymectomy within the first year is proved to possess greater chance of achieving CSR.
ACUTE HAEMORRHAGIC ENCEPHALOMYELITIS MIMICKING CEREBRAL METASTASIS – A DIAGNOSTIC DILEMMA

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Background and Aims: Acute haemorragic encephalomyelitis (AHEM) is the most severe form of acute disseminated encephalomyelitis (ADEM) and is rare. A comprehensive diagnostic workup including a brain biopsy is needed for a definitive diagnosis as it mimics primary and secondary CNS tumours.

Methods: A previously healthy 35 year old man presented with difficulty in swallowing and dysarthria for five days. He had no limb weakness, preceding infections or vaccination. He had a pseudobulbar palsy. Rest of the neurological examination was normal. Routine bloods were normal. CSF was acellular with mild elevation in protein, normal sugar. MRI brain revealed T2 hyperintensities in bilateral frontal and occipital lobes with ring enhancement, perilesional oedema and hemorrhages. Considerations were hemorrhagic metastasis and AHEM. Extensive search of primary malignancy was negative. Brain biopsy revealed demyelination with perivascular lymphocytic infiltration. A diagnosis of demyelinating ‘pseudotumour’ was made. CSF oligoclonal bands were negative. He was treated with IV methylprednisolone pulses (IVMP) and 5 cycles of total plasma exchange (PLEX) which resulted in significant clinical improvement. Oral steroid maintenance was started.

Results: Tumefactive multiple sclerosis or AHEM can mimic and masquerade brain tumours on MRI. Haemorragic lesions made primary CNS lymphoma less likely but haemorragic metastasis was still possible. A brain biopsy is essential in all doubtful cases.

Conclusions: AHEM is a rare clinical entity with a high mortality. A high degree of clinical suspicion is essential for an early diagnosis and treatment with immunotherapy which would be lifesaving.
BILATERAL SINGLE ISOLATED OPTIC NEURITIS WITH TRANSIENT MOG ANTIBODY POSITIVITY – A CASE REPORT

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Background and Aims:: The antibody against the MYELIN OLIGODENDROCYTE GLYCOPROTEIN (MOG-Ab) has been related to optic neuritis, transverse myelitis and acute disseminated encephalomyelitis. Our aim is to report a case of MOG-Ab associated single isolated optic neuritis (SION) with serological follow-up. This report could contribute with the current question about MOG-Ab persistence or negativation and if it could be used as a marker of recurrence and therapy indication.

Methods:: CASE REPORT.

Results:: We present a 33-years-old female that in 2018 presented with pain on eye movement and blurry vision in the right eye and after 2 weeks also in the left eye and no other neurological symptoms. In the acute phase MOG-Ab was positive, magnetic resonance showed contrast enhancement of the right optic nerve, visual evoked potential had bilateral latency delay (bigger on the right eye) and normal optic coherence tomography. After IV following oral glucocorticoids for 1 month, she had complete remission of the symptoms and total recovery of visual function. After 1 year she remained asymptomatic, MOG-Ab was now negative, OCT showed no reduction of the nervous fiber layers and VEP had little improvement on latency. After 3 years, patient showed no recurrence of the symptoms.

Conclusions:: This is a case of a bilateral optic neuritis with benign course without other neurological symptoms that presented no recurrence after 3 years, with negative MOG-Ab at follow-up. This antibody status and titers behavior during the course of the disease could help enlightening as for risk of recurrence and possible treatment.
RETINAL AND CHORIOCAPILLARY VASCULAR CHANGES IN EARLY STAGES OF MULTIPLE SCLEROSIS: A PROSPECTIVE STUDY

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Background and Aims:: Optical Coherence Tomography Angiography (OCTA) abnormalities occur in multiple sclerosis (MS) over the disease course. OCTA investigations at early MS stages are lacking. To investigate vessel density (VD) in macular and papillary regions over two-years after an initial demyelinating event (IDE).

Methods:: VD was analyzed in superficial, deep, choriocapillaris and radial peripapillary plexus at baseline and after one and two years. We also evaluated structural OCT parameters [ganglion cell complex (GCC) and retinal nerve fiber layer (RNFL)] changes.

Results:: Thirty eyes from 15 IDE patients (7 females, 8 males, mean age 28.4 ± 9.6 years) were evaluated. GCC and RNFL thicknesses did not change over After 2 years, we reported a reduced VD in superficial capillary plexus, deep capillary plexus and radial peripapillary capillary plexus respect to baseline (coeff. β = -2.779, p= 0.013; coeff. β = -4.055, p= 0.018 and coeff. β = -2.687, p=0.001; respectively). VD reduction was not associated with EDSS change, relapses occurrence and MRI activity.

Conclusions:: Retinal vascular loss occurs in early stages of MS independently from clinical and radiological disease activity and it is not associated with retinal atrophy. OCTA could represent a novel early biomarker to monitor the MS progression.
LONG-TERM MRI CHANGES IN A PATIENT WITH KELCH LIKE PROTEIN 11-ASSOCIATED PARANEOPLASTIC NEUROLOGICAL SYNDROME

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Background and Aims:: Kelch-like protein 11 (KLHL11) antibodies were first described in 2019, as onconeural antibodies causing autoimmune encephalitis associated with seminoma. Although the clinical features have been reported, long-term observational data is lacking. Our case affords a rare opportunity to study the long term clinical and radiological consequences of Kelch like protein 11-associated paraneoplastic neurological syndrome (PNS).

Methods:: Brain MRI brain was retrospectively assessed. To test for KLHL11 autoantibodies, longitudinal samples from the patient were screened by Phage display Immunoprecipitation and Sequencing (PhIP-Seq). Enrichment for KLHL11 in each sample was generated as a Z-score using the mean KLHL11 RPK generated from 100 Healthy Human plasmas by PhIP-Seq. A threshold of Z-score>3 was considered positive. Immunohistochemistry was performed to identify KLHL11-antigen in seminoma tissue.

Results:: A 49-year-old man presented with 8-year-history of progressive ataxia, sensory hearing loss. Brain MRI revealed progressive brain stem and cerebellar atrophy, and low intensity on susceptibility weighted imaging (SWI) in substantia nigra, red nucleus and dentate nuclei. PhIP-Seq identified positivity for KLHL11 in all samples. Immunohistochemical analysis of seminoma tissue showed anti-KLHL11-antibody positive particles in cytoplasm.

Conclusions:: This study suggests that attention should be paid to the pattern of atrophy and signal changes including SWI considering KLHL11-PNS as differential diagnosis. Investigating the KLHL11 proteins in seminoma tissue may help the diagnosis of KLHL11-PNS if the patient with seminoma has neurological symptoms.
THE USE OF COMBINED THERAPY WITH CFPE AND IVIG IN A PATIENT WITH REFRACTORY STANDARD THERAPY FOR STIFF PERSON SYNDROME

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Background and Aims:: Patient, female 56 years old. The disease debuted in 2015, 1 month after radiiodine therapy for thyrotoxicosis, episodes of stiffness and pain in the muscles of the back. Since March 2018, the patient noted an increase in the stiffness of the axial muscles, fear of walking, and began to use a cane. In May 2018, constant muscular activity in EMG in paraspinal muscles, proximal muscles of the thighs, an increase of anti-GAD antibodies to 46 U/ml, diagnosed Stiff-person syndrome.
Methods: Treatment started with IVIG in the initial dose of 2 g/kg, followed by maintenance courses of 1 g/kg with an injection interval of 4-5 weeks, and symptomatic therapy with benzodiazepine at the
maximum tolerated dose. After the first course of IVIG, effect was noted for 3 weeks. Subsequently, the
effect of the introduction persisted for up to 2 weeks, and was accompanied by traumatic falls. The patient
refused glucocorticosteroid therapy.

**Results:** Since August 2019, before each IVIG course, did cascade filtration plasma exchanges, 2-4
sessions in which 2700 ml of plasma were processed, 300-500 ml of plasma were taken. This therapy
significantly reduced the severity of rigidity, but did not affect the frequency of falls. The effect lasted for 4-
5 weeks.

**Conclusions:** In patients who have been unresponsive to first-line therapies IVIG and plasmapheresis
can be used in combination. According to the results of all the courses carried out, during the observation
period, we were able to achieve an increase in the duration of the period of regression of symptoms up to
4 - 5 weeks.
STUDY OF CLINICAL PROFILE OF AUTOIMMUNE ENCEPHALITIS/ IMMUNOTHERAPY RESPONSIVE ENCEPHALOPATHIES AND THEIR CORRELATION WITH WHOLE BODY F-18 FDG POSITRON EMISSION TOMOGRAPHY

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Background and Aims:: Autoimmune Encephalitis (AE) represents a complex category of diseases with diverse immunological markers, varied clinical manifestations and variable therapeutic outcomes. PET may prove to be a useful biomarker to diagnose and prognosticate the patient of AE. We conducted a systematic, hospital based, prospective study to assess the role of F-18 FDG PET in AE/IRE.

Methods:: Its systematic, hospital based, prospective study to assess the role of F-18 FDG PET in AE/IRE. We attempted to elucidate the pattern of F-18 FDG PET in various type of AE. We studied consecutive patients of autoimmune encephalitis (n=50) diagnosed and treated at a tertiary care center in Northern India.

Results:: Mean age in current study (n=50) was 39.5 ± 19.3 years (Range: 14-76 years). Most common autoantibody was NMDA (36%), followed by LGI-1 and GAD (8% each). PET was abnormal in 28 (63.6%) patients. It showed evidence of hypermetabolism in 9 (20.4%) and hypometabolism in 27 (61.4%) patients. In 8 (18.2%) patients showed evidence of both hypometabolism and hypermetabolism.

Conclusions:: Most common form of AE in North India is NMDA-AE. It is possible to prognosticate AE using clinical, laboratory and neuroimaging criteria. With proper treatment, more than 80% of patients show good clinical recovery.
ANTI-NMDAR ENCEPHALITIS PRECEDED BY INFECTION: SYSTEMATIC LITERATURE REVIEW WITH COMPARISON OF NON-HSV AND HSV RELATED ANTI- NMDAR ENCEPHALITIS.

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Background and Aims:: Antecedent infections are an important trigger for Anti-N-methyl-D-aspartate-receptor (NMDAR) encephalitis (NMDAR-E) with Herpes simplex virus (HSV) being the most recognized. Other infections have also been reported to cause NMDAR-E. We aimed to study the reported cases of non-HSV infections causing NMDAR-E and compare them with HSV-related NMDAR-E.

Methods:: A systemic review of literature was done using key mesh words and newly reported cases (not included in any previous reviews) were included (January 2017 to February 2021). Demography, clinical features, imaging, and treatment details were analyzed.

Results:: We found 51 HSV related and 57 Non-HSV-related NMDAR-E cases described during this period. Viral aetiologies were the commonest infection-related triggers for NMDAR-E (n=92/108, 85%). Non-HSV-related NMDAR-E triggers included bacterial (15.78%), other viral (71.92%), parasitic (3.5%), and mixed (8.77%) infections. Non-HSV-related NMDAR-E cases as compared to HSV-related NMDAR-E had a younger median age of onset (21 vs 33 years), more psychiatric, autonomic, and sleep disturbances (73% vs 35%, 19% vs 7%, 44% vs 22 % respectively), and better outcome (complete recovery in 64% vs 36%). Contrarily, HSV-related NMDAR-E had more cognitive disturbances, headache and hypotonia as symptoms (57% vs 37%, 26% vs 2%, 13 % vs nil), and more disabilities (partial recovery: 61% vs 28%) MRI brain showed normal or diffuse brain involvement in 57% in the former group while temporal lobe involvement was seen in 70% of the latter.

Conclusions:: Non-HSV infections are also important triggers of NMDAR-E. Non-HSV-related NMDAR-E has a slightly different clinical profile and better prognosis as compared to HSV-related NMDAR-E.
Background and Aims:: Bariatric surgery is an efficient treatment to achieve significant weight reduction in patients with morbid obesity. However, neurological complications after bariatric surgery are not uncommon and had been extensively discussed including cases of GBS. We are presenting cases of GBS which occurred after bariatric surgery on different postsurgical stage in our cohort with literature review aiming to stratify GBS development risk after bariatric surgery.

Methods:: Tawam hospital bariatric surgery registry was used to select and review neurological complications with emphasis on GBS development after surgery. We additionally completed a search in PubMed for published GBS cases after bariatric surgery from January 2010 till January 2020 with detailed review of demographics, clinical and electrophysiological presentations, as well as response on treatment and pattern of clinical recovery.

Results:: We were able to identify two cases with rapidly progressive GBS in our cohort and seven GBS published cases developed after bariatric surgery which were found in the Pub Med. All GBS cases after bariatric surgery are going to be presented and discussed in details including a possible risk stratification for GBS development.

Conclusions:: Causative role of bariatric surgery in development of GBS still unclear; however nutritional component after bariatric surgery may play role and most likely can trigger autoimmune and inflammatory mechanisms which may lead to development of acute inflammatory polyneuropathy alone or/and in a combination with malnutritional conditions. Inflammatory component should not be ignored in case of post-bariatric neurological complications and their management.
ADULT PRIMARY CENTRAL NERVOUS SYSTEM VASCULITIS. A CASE-SERIES.

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Background and Aims:: Adult primary central nervous system vasculitis (PCNSV) is a rare and challenging disorder of the brain and spinal cord arteries, which can benefit from immunotherapy. The histological demonstration of vasculitis allows a defined diagnosis; however, brain biopsy is sometimes not feasible, and diagnostic suspicion should drive treatment. We report four cases.

Methods:: All cases underwent extensive blood and cerebrospinal fluid (CSF) exams and MRI, angiography was performed in three (#1-3), brain biopsy in one (#4). The follow-up ranged between one and five years.

Results:: Three otherwise healthy women between 43 and 47 years old (#1-3) and a 69 years old man with peripheric atherosclerotic arteriopathy and alcoholic hepatopathy (#4) presented in ER for transient acute neurological deficit associated with headache (#2, #3) or progressive focal motor and sensory deficit (#1, #4). All women had subcortical watershed infarcts and angiographic evidence of cerebral artery stenosis; one presented post-contrast enhancement of the artery wall (#1), another showed extracranial internal carotid dissection and mild subarachnoid haemorrhage (#3). The man had a subcortical tumour-like lesion. CSF exam was normal except for intrathecal synthesis of oligoclonal bands (is-OCBs) in three cases (#2-4). Brain biopsy showed perivascular leucocytes infiltrate. Corticosteroids and cyclophosphamide were started based on radiological (#1), radiological and CSF (#2-3), or CSF and histological data (#4). During follow-up, all patients presented a clinical improvement without relapses.

Conclusions:: After accurate differential diagnosis, a careful imaging evaluation and CSF analysis also for is-OCBs can support the diagnostic suspect of PCNSV and therapeutic decisions.
ISOLATED IMBALANCE DUE TO BILATERAL VESTIBULAR FAILURE FOLLOWING IMMUNE CHECKPOINT INHIBITOR ADMINISTRATION

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Background and Aims: T-cell targeted Immune Checkpoint Inhibitors (ICI) has revolutionised the field of oncology in the last decade and are used to treat a variety of cancers.

Methods: Here, we report two patients who developed acute isolated bilateral vestibular failure following use of ICI therapy and postulate that such presentations where a gait disorder may be the sole presenting feature, may be under-reported.

Results: We show how the vestibular function can be documented using video head impulse testing to objectify change over time.

Conclusions: Whilst the exact means by which ICI administration may lead to cranial mononeuropathy remains unknown, removal of key negative immune regulators is thought to be contributory. It has been suggested that inner ear melanocytes could be a target of an autoimmune process in patients with melanoma treated with ICIs, leading to production of antibodies that cross-react with both the melanoma cells and the labyrinth melanocytes, leading to audiovestibular loss. Neurologists involved in the management of oncology patients receiving ICI should be aware of isolated bilateral vestibular loss as a potential adverse event, with significant functional consequences for a patient’s gait and balance.
NEUROMYELITIS OPTICA SPECTRUM DISORDERS IN THE ELDERLY

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Background and Aims:: Introduction. Neuromyelitis Optica is a severe autoimmune inflammatory demyelinating disease that affects mainly the spinal cord and optic nerves with a young female predilection. It can present with a severe neurological presentation from the beginning with a poor prognosis. However, it is rare to see it in elderly subjects with aggressive and insidious onset of symptoms. Objective. Our cases highlight the varied clinical presentations of NMOSD and we believe that the diagnosis of NMOSD should be considered in elderly patients in the appropriate clinical setting despite the presence of unconventional symptoms.

Methods:: Observation In this work, the authors report late cases of Devic's neuromyelitis Optica in two women aged 66 and 71 years whose neurological examination showed a complete spinal cord syndrome and a tetrapyramidal syndrome respectively. MRI of the spinal cord showed an extensive myelitis appearance. Anti-NMO and anti-MOG IgG antibodies in the blood were positive. Our patients received a high-dose corticosteroid bolus for 5 days with the protocol of Rituximab 1g per course and motor rehabilitation sessions.

Results:: The evolution is marked by a clear clinical improvement.

Conclusions:: Conclusion. Neuromyelitis Optica is an autoimmune pathology that is exceptional in the elderly and has a poor prognosis, hence the interest in evoking it in the presence of a serious and insidious neurological presentation in order to start treatment early.
CD8 T CELL-MEDIATED CEREBELLITIS DIRECTED AGAINST PURKINJE CELL ANTIGEN AFTER IPILIMUMAB FOR SMALL CELL LUNG CANCER

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Background and Aims:: Immune checkpoint inhibitors are increasingly associated with central nervous system complications, and clinical presentation may resemble that of classical paraneoplastic syndromes. Several immune-mediated cerebellar syndromes have been reported in this context, and histological study is now needed to reveal immunological mechanisms and determine whether these are similar to paraneoplastic cerebellar degeneration.

Methods:: We present a case of cerebellitis in a 63-year-old man who received ipilimumab (cytotoxic T-lymphocyte-associated protein 4 inhibitor) for small cell lung cancer as part of a phase II trial. After death, a post-mortem examination was performed followed by immunohistochemical study of the brain.

Results:: The patient developed a cerebellar syndrome 37 weeks after ipilimumab. Contrast-enhanced magnetic resonance imaging of the brain and spinal cord was normal. Cerebrospinal fluid was acellular with normal glucose but a raised protein and paired oligoclonal bands. Baseline weakly positive anti-Yo antibody titres were unchanged following treatment. He deteriorated despite immunosuppressive treatment and died during week 39. Histology revealed that pathology was limited to the cerebellar cortex, consisting of a patchy CD8 T cell infiltrate spatially corresponding to areas of Purkinje cell loss. There was evidence of CD8 polarisation towards Purkinje cells and Bergmann astrocyte activation. By comparison, CD20-positive B cells were sparse.

Conclusions:: CD8 T cell-mediated cerebellitis after ipilimumab may represent early pathology seen during paraneoplastic cerebellar degeneration. This case highlights the need for continued vigilance with CTLA-4 inhibitors, especially when anti-neuronal antibodies are present at baseline. Treatments which suppress T cell responses merit further study.
IMPACT OF NEUROMYELITIS OPTICA SPECTRUM DISORDER ON QUALITY OF LIFE: ASSESSING THE PATIENTS’ PERSPECTIVE

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Background and Aims:: Symptomatology and number of attacks in neuromyelitis optica spectrum disorder (NMOSD) reduce patients’ health-related quality of life (HRQoL). Limited information is available from patients’ perspective in Spain. The aim of this study was to assess the impact of NMOSD on HRQoL from the patients’ perspective.

Methods:: A non-interventional, cross-sectional study was conducted in 13 neuroimmunology clinics in Spain. NMOSD patients (2015 Wingerchuk criteria) were included. Expanded Disability Status Scale (EDSS), SymptoMScreen (SyMS), 29-item Multiple Sclerosis Impact Scale (MSIS-29), 8-item Stigma Scale for Chronic Illness (SSCI-8), Beck Depression Inventory-Fast Screen (BDI-FS), Pain Effects Scale (PES) and Fatigue Impact Scale for Daily Use (D-FIS) were used to assess disability, symptom severity, HRQoL, stigma, mood, pain and fatigue, respectively. Outcome measures associations were analysed using Pearson correlation.

Results:: Seventy-one patients were studied (mean age: 47.4 years ±14.9, 80.3% female, mean disease duration: 9.9 years ±8.1, median EDSS: 3.0 [interquartile range: 1.5-4.5]). Mean physical and psychological MSIS-29 sub-scores were 41.9±16.8 and 20.9±8.3, respectively. SyMS mean scores were highest for fatigue (2.4±1.8) and bodily pain (2.2±1.8). Stigma prevalence was 61.4% (n=43) and 44.3% (n=31) of patients had depressive symptoms. Physical MSIS-29 showed significant correlation with SyMS (rho=0.856, p<0.0001). BDI-FS was correlated with SyMS, psychological MSIS-29, PES, D-FIS and SSCI-8 (rho=0.621, 0.714, 0.664, 0.663, 0.613, respectively, all p<0.0001). Perception of stigma predicted concurrent depression (OR=1.32; 95% CI: 1.13-1.55, p=0.0004).

Conclusions:: NMOSD poses a significant burden on patients’ HRQoL from their perspective. Assessing patient-centered outcomes may be crucial to achieve a holistic approach of disease allowing early interventions.
COMMON PARANEOPLASTIC NEUROLOGICAL SYNDROMES IN PAKISTAN: CLINICAL AND IMMUNOLOGICAL ASPECTS

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Background and Aims:: To determine the frequency and clinical features associated with anti-neuronal antibodies in patients suspected of paraneoplastic neurological syndromes and autoimmune encephalitis in a tertiary care hospital in Islamabad, Pakistan.

Methods:: After approval from IRB & ethics committee, we reviewed laboratory records of patients suspected of paraneoplastic syndromes (PNS) and autoimmune encephalitis, from February 2019 to February 2021. Indirect Immunofluorescence technique was used for autoimmune encephalitis and Immunoblot for PNS. The clinical features, response to treatment and associated malignancies were recorded for analysis.

Results:: A total of 46/524 patients (8.7%) had immune encephalitis; mean age 32.07 years; 58.6% were females. Anti-NMDAR antibodies were present in 31/46; Anti-Caspr2: 7/46; Anti-LGI1: 6/46 and Anti-GABA-B receptor antibodies in 2/46. 28/46 with complete clinical data were included for clinical correlation. NMDAR encephalitis was the presentation in 18/28; limbic encephalitis in 9/28 and neuromyotonia in 1/28. 23/28 patients responded to immune-modulatory therapies. Of 357 tested for antibodies for PNS, 25 were positive (7%). Mean age 53.4 years; 52% were female. 7/25 patients had Anti-Amphysin antibodies; Anti-Titin: 5/25; Anti-Yo: 3/25; Anti-SOX1: 2/25; Anti-CV2: 1/25. Multiple antibodies: 5/25 patients. Eleven patients with insufficient clinical data were excluded. Common PNS were myasthenia gravis: 3/14; sub-acute cerebellar degeneration: 3/14; limbic encephalitis: 3/14; encephalomyelitis: 2/14, stiff-person syndrome: 2/14; LEMS in 1/14. Most responded poorly to treatment (9/14); 6/13 patients had malignancies.

Conclusions:: NMDAR antibody encephalitis was the most frequent immune encephalitis and had a favourable response to immunotherapy. Paraneoplastic neurological syndromes were less responsive to treatment, but helped in early tumor detection.
SEVERE ACUTE POLYRADICULONEURITIS REVEALING SYSTEMIC LUPUS ERYTHEMATOSUS

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Background and Aims:: Introduction Systemic lupus erythematosus is a common disease with extremely heterogeneous neurological manifestations in its clinical expression. However, few cases have been reported in the last 50 years where the initial manifestation of SLE is Guillain-Barré syndrome. Our work highlights the importance of SLE as a potential etiology in a patient with acute polyradiculoneuritis.

Methods:: Observation A 41-year-old woman, with a history of three miscarriages and skin photosensitivity, presented with sudden onset symptomatology of synchronous and symmetrical ascending functional impotence of both lower limbs 20 days before admission. Clinical examination revealed a dyspneic patient with a peripheral neurogenic syndrome predominantly distal to the 4 limbs with generalized myxedema associated with alopecia. Electroneuromyography showed an axonal motor polyradiculoneuropathy more marked in the two lower limbs. Biological abnormalities were in favor of SLE. The diagnosis of acute Guillain-Barré type PRN associated with lupus disease was retained. The patient received a bolus of methyl-prednisolone, monthly courses of cyclophosphamide 1 g, and synthetic antimalarials such as hydroxychloroquine (Plaquenil) 400 mg daily.

Results:: The evolution is marked by a clear clinical improvement.

Conclusions:: Conclusion: Neurological manifestations in lupus disease are common; whereas the form of acute polyradiculoneuropathy is very rare with a risk of vital engagement prognosis. Early diagnosis and management are essential.
UNCOMMON ASSOCIATION OF NMDA RECEPTOR ENCEPHALITIS WITH INTRACRANIAL GERM CELL TUMOUR

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Background and Aims:: N-methyl-d-aspartate receptor encephalitis (NMDARE) has significant association with ovarian teratoma; meticulous search and removal of the same is a key step in the management. We describe challenges in the management odyssey of a 21-year-old lady with NMDARE.

Methods:: Clinical features, brain MRIs, NMDA-antibodies in serum and/or cerebrospinal fluid (CSF) and other investigations during the course of 44 months were reviewed

Results:: This patient presented with seizures, abnormal behaviour and impaired memory of five months duration. Brain MRI showed ill-defined enhancing hyperintensities in cingulate gyri, corpus callosum, and brainstem. NMDA-antibodies were weakly positive in serum. PET-CT showed focally restricted diffusion in right ovary; no lesion was noted on ultrasound and biopsy was denied. She improved with steroids. After five months, she developed apathy and catatonia. Plasmapheresis was given and azathioprine was added. At ninth month, she improved significantly and remained well except for seizure-recurrence at 25th month. Evaluation on four occasions showed that serum NMDA antibodies and brain MRIs were persistently abnormal, but pelvic ultrasound was normal. At 37th month, she discontinued treatment and developed severe relapse in 41st month leading to bedridden state. Brain MRI at 44th month showed remarkable increase in lesion load with diffuse nodular meningeal enhancement (sugar-coating appearance). While serum NMDA antibodies were weakly positive, CSF showed strong positivity for NMDA antibodies. Biopsy from frontal lesion showed features of germ cell tumour.

Conclusions:: While ovarian teratoma is a well-known association with NMDARE, intracranial spread of germ cell tumour is uncommon. Early tissue diagnosis is warranted for diagnosis and appropriate treatment.
PICK YOUR POISON: NEUROBEHÇET OR CENTRAL NERVOUS SYSTEM PARANEOPLASTIC SYNDROME?

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Background and Aims:: The diagnosis of rhomboencephalomyelitis is often challenging, with a wide variety of etiologies to be considered, some potentially fatal in the absence of early diagnosis and treatment, like Neurobehçet and paraneoplastic encephalomyelitis.

Methods:: A case of a 52-year-old patient with a challenging differential diagnosis of rhomboencephalomyelitis is presented.

Results:: A 52-year-old male Portuguese patient, with history of recurrent uveitis, was admitted to the Emergency Department with a subacute progressive left hemiparesis, vertigo and gait instability. On the neurological examination, the patient displayed left hemiparesis and hypoesthesia, scanning speech, appendicular and gait ataxia. Neural axis imaging with MRI was conducted, revealing an asymmetrically bilateral infiltrative lesion, with extension from the diencephalon to the lateral cervical cord. CSF analysis revealed hyperproteinorachia (58mg/dl) and pleocytosis (56.0 leukocytes/uL), with mild mononuclear predominance. Blood and CSF serologies (namely for Listeria monocytogenes) and antineuronal antibodies were negative. A renal carcinoma on the right kidney found on a CT scan and a positive HLA type 51 assay suggested two possible diagnoses: paraneoplastic rhomboencephalomyelitis versus Neurobehçet. A cycle of Methylprednisolone IV was started followed by oral immunosuppressors and the tumor was surgically removed, not requiring adjuvant treatment. At follow-up three months later, marked clinical and imaging improvement was reported. Clinical and paraclinical data suggested Neurobehçet as the most likely diagnosis.

Conclusions:: The broad clinical spectrum, the absence of validated diagnostic criteria and the lack of specificity of ancillary diagnostic testing can dictate the complexity of the diagnosis of a rhomboencephalomyelitis.
OCULAR MYASTHENIA GRAVES IN A PATIENT WITH COVID-19; NEUROLOGICAL OVERVIEW OF AUTOIMMUNE COMPLICATIONS OF COVID-19

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Background and Aims:: COVID-19 is a highly contagious pathogen caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Recent studies have shown that COVID-19 shares similarities with autoimmune diseases in clinical manifestations, immune responses, pathogenic mechanisms and the presence of autoantibodies. Also, some patients have been reported to develop autoimmune diseases such as Guillain–Barre syndrome and Myasthenia Graves (MG) after COVID-19. MG is an autoimmune disease of the neuromuscular junction, affecting ocular, bulbar, respiratory and skeletal muscles. We report an ocular MG developing secondary to COVID-19 infection in a 45-year-old female patient on the 10th-day of COVID-19 infection. She described pain and droopy eyelid in the right eye. Her complaints were increased during the day, especially towards the evening. A neurological examination revealed semi-ptosis in the right eye. There was no blurred or scarcity of vision and no diplopia. Other neurological examination was normal. Her cranial magnetic resonance imaging (MRI), orbital MRI and MRI angiography were evaluated as normal in terms of intracranial pathologies. Serum hemogram, biochemical tests, serological tests, coagulation tests and electrophoresis tests were completed normally. We evaluated the patient in aspects of MG with these clinical findings, and serum and electrophysiological test were performed. Serum acetylcholine receptor antibody (AChR) test resulted positive (5.58 nmol/L). Voluntary single fiber EMG showed increased jitter values that were compatible with motor endplate dysfunction. Thymus gland computed tomography in terms of hyperplasia or thymoma evaluated as normal. The patient was diagnosed with ocular myasthenia and deltacortil (5 mg tb) treatment was started.

Methods:: CASEREPORT
Results:: CASEREPORT
Conclusions:: CASEREPORT
ANTI NMDA ENCEPHALITIS: A RARE CAUSE OF TEMPORAL EPILEPSY

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Background and Aims:: rare, unrecognized and treatable entity.
Methods:: 15-year-old patient, who presented in a rapidly progressive way olfactory hallucinations, paroxysmal, a few days later, appearance of contact breaks with automatisms. Examination: T ° 38.2, profuse sweating and oral dyskinesias. MRI: hyper signal in left temporo-insular. EEG: nonspecific slow waves CSF: high proteinorachia (0.95g / l) normal, cytology: 43 lymphocyte-like elements, presence of oligoclonal bands of IgG. The paraneoplastic assessment is negative NMDA antibody assay were positive in CSF. The patient received corticosteroids by infusion (01g /day for 05 days), then 05 courses of immunoglobulins. The evolution has been towards almost total clinical improvement.
Results:: An infectious origin is quickly eliminated by the negativity of the serologies and the PCR. The diagnosis of dysimmune encephalitis is then suspected, especially anti NMDA (young age, cephalic dyskinesias...), is retained after immunological analysis. Anti-NMDA encephalitis mainly affects women (80%), with an onset between age 18 and 35, first manifests itself in a psychiatric. Then neurological symptoms set in (epileptic seizures, orofacial dyskinesias...). The seizures are most often generalized, tonic-clonic but also complex partial, or secondarily generalized. The study of CSF is often inflammatory, with oligoclonal bands.. Brain MRI finds a hyper signal in the hippocampus, or temporo-insular, or frontal, or extra limbic. EEG can reveal delta brush or rhythmic slow wave anomalies. It is also necessary to know how to look for an ovarian teratoma.
Conclusions:: Focal epilepsy, of recent onset and explosive, of unexplained etiology, especially of the temporal type and drug-resistant, should encourage the search for autoantibodies.
Background and Aims:: We present the case of a male patient with a central nervous system germinoma that simulated three clinical syndromes of NMOSD, so we consider it necessary to screen him in case of therapeutic failure to initial treatment with steroids. A 19 male years old, previously healthy, In May 2019, he presented a sudden decrease in bilateral visual acuity, worsening the right eye. A cranial MRI was negative, and he starts prednisone 25 mg QD, with partial improvement. Despite this therapeutic, he continued with decreased visual acuity. In July 2020, begins with hiccups and cough that later became self-limiting. A quick examination by gastroenterology does not reveal structural alteration.

Methods:: In July 2020, he presented multiple episodes of hiccups and cough that later self-limited. In October, he started with hiccups, nausea, cough, and dysphagia being refractory to symptomatic treatment, in addition to worsening in visual acuity. Serum anti-aquaporin-4 antibodies were negative. In spite of this, he was treated with pulses of methylprednisolone, without response. To December, he developed amaurosis of the right eye and shadow perception in the left eye and multidirectional nystagmus exacerbated by the left gaze version. In funduscopy he presented bilateral optic atrophy.

Results:: In the imaging follow-up with MRI and PET, a lesion persists in the right optic nerve. Neurosurgery decided to approach a lesion biopsy. Histopathology was matched with germinoma. Lumbar puncture showed levels of human chorionic gonadotropin in 69.09 (>2.63 UI/ml).

Conclusions:: CNS germinoma simulated an NMOSD. The patient is under chemotherapy (ifosfamide and etoposide) and radiotherapy.
GRANULOMATOUS ANGIITIS OF THE CENTRAL NERVOUS SYSTEM: CLINICAL AND IMAGING PROFILE AND RESPONSE TO TREATMENT

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Background and Aims:: Granulomatous angitis of central nervous system (GACNS) is a rare idiopathic necrotizing vasculitis. Clinical manifestations are heterogeneous and diagnosis is challenging. We aim to describe the clinical course and outcome in patients of biopsy-proven GACNS.

Methods:: Data on clinical and imaging features, histological findings, and relevant investigations of four patients seen in a single neurology unit were compiled retrospectively.

Results:: All subjects were men. Age at presentation ranged from 19 to 39 years. Duration of symptoms ranged from 0.5 to 60 months. Initial symptom was headache (n=2), facial weakness (n=1), and progressive paraparesis (n=1). Clinical profile included encephalopathy (n=2), cognitive decline (n=2), headache (n=2), seizures (n=1), facial palsy (n=1), paraparesis (n=1), hemiparesis (n=1) and bladder dysfunction (n=2). Brain MRI showed multifocal signal changes in cerebral, cerebellar, and brainstem regions with hemorrhages and variable enhancement in all. Spine MRI showed longitudinally extensive hyperintensity with patchy enhancement in one patient. Cerebrospinal fluid analysis showed pleocytosis in all (10 to 200 cells/cu.mm.) and protein ranged from 40 to 180 mg/dl. Meningocortical biopsy showed perivascular lymphocytic cuffing, epithelioid cell granulomas and multinucleate giant cells with normal intervening parenchyma and hemosiderin foci. All patients received steroid and steroid-sparing agents (cyclophosphamide=three, azathioprine=one). Duration of follow-up ranged from 1 to 40 months. Outcome at last follow-up was: complete improvement in two, partial improvement in one and relapse in one.

Conclusions:: GACNS causes extensive brain involvement and clinical profile is non-specific. Meningocortical biopsy helps in establishing a definitive diagnosis. Outcome is good in appropriately treated patients of GACNS.
Background and Aims:: Muscle-specific kinase (MuSK) myasthenia gravis (MG) is often a more severe form of MG that presents with a rapid onset and prominent bulbar symptoms. Today, the diagnosis of MuSK MG is heavily reliant on the antibody (Ab) status of the patient. In most laboratories worldwide, the Abs are measured by radio immune precipitation assay (RIPA). We have developed another testing platform using surface plasmon resonance (SPR) technology. Our aim was to measure the clinical sensitivity and specificity for two different MuSK Ab assays.

Methods:: To assess clinical utility, we are describing a retrospective clinical evaluation of 987 AchR Ab negative samples that have been measured for MuSK Ab by the two different techniques.

Results:: 132 of the 987 AchR Ab negative samples were either positive or borderline for MuSK Abs by one of the 2 methods. Every final diagnosis of the patients associated with these samples was reviewed in detail. Also, 167 randomly selected patients who tested negative with both tests were assessed for clinical diagnosis. The RIPA assay showed to be 49% to 58% sensitive depending on the criteria of diagnosis used and 89-92% specific. The SPR assay is 68-79% sensitive and 67% specific. When both assays are in congruence the specificity is 100%

Conclusions:: The RIPA assay is the gold standard, but the SPR technique was more sensitive than the RIPA. Unfortunately, the SPR technique is less specific. SPR is helpful to follow antibody titer and evaluate treatment response. A prospective study of its usefulness in these conditions is in planning.
ALTERED IL-33/SST2 AXIS IN GUILAIN BARRE SYNDROME AND ITS FUNCTIONAL ROLE IN DISEASE ACTIVITY

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Background and Aims:: Interleukin -33 (IL-33) and its soluble receptor (sST2) regulate Th1/Th2 immune responses; the altered activity of IL-33/sST2 leads to the development and severity of various immune-mediated diseases. This study is aimed to explore the role of IL-33/sST2 axis in Guillain Barre Syndrome (GBS).

Methods:: In this study, 178 patients with GBS and 185 healthy subjects were recruited. Three single nucleotide polymorphisms (SNPs) of Il33 gene (rs16924159; rs7044343; rs1342336) and 3 SNPs of Il1rl1 gene (rs10192157, rs1041973, rs10206753), coding for sST2 were genotyped in all the subjects by TaqMan Allelic Discrimination Assay. Besides, plasma levels of IL-33 and sST2 were measured in a subset of patients (n=80) and healthy subjects (n=80) by ELISA.

Results:: The frequencies of the alleles and the genotypes of the SNPs of Il33 and Il1rl1 genes did not differ significantly between patients with GBS and healthy subjects. Further to this, none of these SNPs correlated with antecedent infections, disability scores or electrophysiological subtypes of GBS. The plasma levels of IL-33 were undetectable in all the studied subjects. However, the plasma levels of sST2 were significantly elevated in patients with GBS compared to healthy subjects (24,934.31 ± 1.81 pg/ml vs 12,518.97 ± 1.51 pg/ml, p<0.001). The levels of sST2 showed a significant correlation with the disability scores at the peak of neurological deficit in patients with GBS.

Conclusions:: The sST2 levels are significantly elevated and correlate with disease disability in GBS. IL-33/sST2 axis may play a pivotal role in the autoimmune origin of GBS.
MEDIATORS OF TOLL-LIKE RECEPTOR (TLR) PATHWAY AS GENETIC DETERMINANTS OF GUILLAIN BARRE SYNDROME

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Background and Aims:: Toll-like receptor (TLR) pathway is crucially involved in initiating innate immune response against microbes. Dysregulation of TLRs can exacerbate immune-inflammatory responses and genetic variations within tlr genes contributes to differential risk to infection. This study is aimed to examine the role of genetic variations within tlr2, tlr3, and tlr4 genes as well as genes coding for intracellular signalling molecules such as myd88, nf-kb1, ikbα, traf3, traf6, trf, and irf3 of TLR pathway.

Methods:: In this prospective study, 150 patients with GBS and 150 healthy subjects were recruited. Fourteen polymorphisms, two from each of tlr2 (rs3804099; rs111200466), tlr3 (rs3775290; rs3775291), tlr4 (rs1927911, rs11536891), myd88 (rs7744, rs4988453), and one from each of nf-kb1 (rs28362491), ikbα (rs696), traf3 (rs12147254), traf6 (rs4755453), trf (rs8120) and irf3 (rs2304204) were genotyped in all the subjects either by PCR-RFLP or TaqMan Allelic Discrimination Assay.

Results:: Statistically significant differences of genotype frequencies of rs111200466 and rs3804099 of tlr2, rs3775290 of tlr3 and rs11536891 of tlr4 were observed between GBS patients and healthy controls. The Del/Del genotype rs111200466 (p<0.001) and CT genotype of rs3804099 (p=0.002) of tlr2 gene were significantly associated with the risk of GBS. The TT genotype of rs3775790 of tlr3 (P<0.001) and CT genotype of rs11536891 of tlr4 (P<0.001) genes were also found to confer increased risk to GBS. Gene-gene interaction analysis by Multifactor Dimensionality Reduction (MDR) analysis suggest a significant combined effect of tlr2, tlr4 and ikbα genes on the risk of GBS.

Conclusions:: The genes of the TLR pathway could serve as important genetic determinants of GBS.
PROBABLE AUTOIMMUNE ENCEPHALITIS PRESENTING WITH EPILEPSY, FEVER AND AGEUSIA: A POSSIBLE COVID-19-RELATED EVENT?

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Background and Aims:: Encephalitis is an acute inflammation of brain parenchyma, clinically characterized by confusional state and cognitive decline, fever, headache, and an altered level of consciousness. Encephalitis is typically viral or autoimmune. Aim of the study is to discuss a case of autoimmune encephalitis with anosmia and epileptic seizures at clinical presentation.

Methods:: Blood and CSF analysis, electroencephalography and brain 18 FDG PET-MRI were done. Cognitive status was tested by Mini Mental State Examination.

Results:: We report on a 60-year-old man with an episode of incongruos speech and behaviour, spatial disorientation, diarrhea, ageusia and hyperpyrexia occurred in December 2019. Blood examination was normal for infective and inflammatory diseases. At admission EEG showed irritative anomalies in the left frontal-central regions. CSF analysis showed 12 WBC and no evidence of infection; brain MRI was normal. The patient was treated with acyclovir with partial benefit. In the following months he had apathy, deflected mood and drowsiness. In November 2020 a new episode of confusion occurred, with transitory visual field impairment and headache. This time he was tested with MMSE, with a score of 25/30. A new brain MRI and EEG, in February 2021, were unchanged. Brain FDG-PET/MRI revealed slight hypermetabolism of the left amygdala. Anti AMPAR, GABA R, GAD, VGKC and antineuronal antibodies were negative. CSF was normal a part from presence of oligoclonal bands. CSF anti COVID-19 spike protein antibodies assay was negative.

Conclusions:: A diagnosis of autoimmune encephalitis with unknown antibodies was made and possible association with COVID-19 infection was deemed unlikely.
Background and Aims:: Rheumatoid arthritis is a chronic systemic autoimmune disorder, leading to joints` inflammation and their destruction. Extra articular manifestations are described in about 20% of patients with rheumatoid arthritis. Rheumatoid meningitis (RM) is a very rare severe complication with CNS involvement. The severity and lethality of rheumatoid meningitis is determined by its challenging diagnosing due to multiplicity of clinical symptoms and takes 60% by Mélanie Trabelsi et al, in spite of treatment. The purpose of this case study is to spread the social awareness about rheumatoid meningitis.

Methods:: Contrast enhancing brain MRI, blood tests.

Results::
A young woman of 22 years old admitted to the outpatient clinic complaining of a 2-day history of the unilateral neck and occipital area headache on the right. The pain was associated with photophobia, subfebrile temperature and arthralgia. Physical examination: mildly positive meningeal signs, brisk tendon reflexes. Head magnetic resonance imaging (MRI) and computed tomography scans were normal. Blood tests: red blood cells 4.07 x 10^12/l, ESR 58 mm per hour, thrombocytes of 504x10^9/l, white blood cells 11.29, CRP 23.73 mg/l, ASO 265 IU/ml, rheumatoid factor 14.73 mg/l, other blood tests were
unremarkable. Gadolinium-enhanced head MRI showed right hemisphere pachymeningeal and leptomeningeal enhancement. The patient was diagnosed with: Aseptic rheumatoid meningitis. The treatment included prednisolone with complete improvement.

**Conclusions:** We present a case of unilateral RM, an extremely rare neurological complication of first diagnosed rheumatoid arthritis. The improvement was noted after two week of per os treatment with 8 mg/day prednisolone.
PARANEOPLASTIC AUTOIMMUNE AUTONOMIC GANGLIONOPATHY AS A DEBUT OF A BLADDER UROTHELIAL CARCINOMA: A CASE REPORT

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Background and Aims:: Autoimmune autonomic ganglionopathy (AAG) is a rare immune-mediated disorder associated with anti-α3 subunit of the ganglionic-type nicotinic acetylcholine receptor (anti-gAChRα3) antibodies, which bind to the acetylcholine-receptor in autonomic ganglia (parasympathetic and sympathetic), leading to autonomic failure. This disorder is mostly associated with viral infections, but it can also be associated with systemic malignancies. Here, we report the first case of a paraneoplastic autonomic ganglionopathy as a debut of a bladder urothelial carcinoma.

Methods:: Case report.

Results:: A 44-year-old man, without medical history of interest, went to the emergency department because of blurry vision, eye and mouth dryness, constipation and orthostatic hypotension, for the last 2 weeks. A drop in blood pressure (BP) upon standing was documented [100/60 mmHg (decubitus) vs. 80/50 mmHg (sitting)]. Blood tests, chest x-ray, brain-MRI, cerebrospinal fluid and electroneuronography were unremarkable. Electrochemical skin conductances were decreased in the feet. Serological examinations were positive for anti-gAChRα3 antibodies. A full-body computed tomography showed a bladder tumor, which was surgical treated by transurethral bladder resection. The pathology showed a low grade non muscle invasive bladder urothelial papillary carcinoma. After tumor resection and treatment with intravenous immunoglobulins and corticosteroids, the patient gradually improved.

Conclusions:: Subacute panautonomic failure can be the debut of systemic malignancies. As far as we know, this is the first case report showing a paraneoplastic autonomic ganglionopathy as debut of bladder urothelial carcinoma. This case highlights the importance of a systemic study to rule out the presence of cancer when AAG is present.
INFECTIOUS LESIONS OF THE INSULA ASSOCIATED WITH EXTREME SINUS BRADYCARDIA: REPORT OF THREE CASES

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Background and Aims:: The relationship between ischemic lesions in the insula and alterations of the heart rhythm due to autonomic nervous system dysfunction is known. However, the association with infectious (viral or bacterial) lesions has been poorly reported in the literature. Here, we described 3 cases of sinus bradycardia associated with infectious lesion of the insula.

Methods:: Case series.

Results:: Case 1: A 36-year-old man went to the emergency department because of 6 repetitive transient-losses-of-consciousness on the same day along with headache. During a new syncope, a sinus bradycardia at 35 bpm with asystole (> 5 seconds) was documented, and a transitional pacemaker was implanted. Due to fever, a lumbar puncture was performed, showing herpes-simplex-virus-DNA. MRI showed linear uptake in the right insula. After acyclovir treatment, the electrocardiographic alterations disappeared. Case 2: A 54 year-old man went to the emergency department because of headache and fever and a sinus bradycardia of 40 bpm was documented. A lumbar puncture showed herpes-simplex-virus-DNA. MRI showed linear uptake in the right insula. After acyclovir and foscarnet treatment, the heart rate returned to normal. Case 3: A 54 year-old woman, diagnosed with acute pneumococcal meningitis caused by bilateral otitis media, developed a bradycardia of 33 bpm, without any other alteration in ECG. Echocardiogram was normal. A brain MRI showed purulent material in the context of cerebritis at right insular level. After antibiotic treatment, the bradycardia disappeared.

Conclusions:: Clinicians should be aware that viral or bacterial lesions in the insula could lead to cardiac arrhythmia due to central autonomic nervous system dysfunction.
RELATIONSHIPS BETWEEN RESTING AND REFLEXIVE MEASURES OF HEART RATE VARIABILITY (HRV)

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Background and Aims:: Resting HRV is an important diagnostic and prognostic tool in the evaluation of autonomic dysfunction. Resting and reflexive HRV are markers of the autonomic nervous system, however, their relationship has largely been described only in healthy and diabetic patients. This relationship has not been explored in patients with neurologic disease or in medically complex patients. This study aims to investigate the demographic, medical, neurologic, and autonomic correlates of resting HRV in order to further understand factors that may be considered potential confounders in studies of resting HRV.

Methods:: In this retrospective study of a diverse, urban population (50.2% female, 45% HIV+, median age 50 (IQR 41,57)), results from autonomic function testing (AFT) of 209 patients were analyzed.

Results:: Moderate correlation was found between both root-mean square of differences of successive RR intervals (rMSSD) and percent of differences of adjacent RR intervals >50ms (pNN50) and heart rate during deep breathing (HRDB) (r=.53, p<0.0005), Valsalva ratio (VR) (r=.45, p<0.0005), and age (r=-.25, p<0.0005). No correlation was found between pNN50/rMSSD and the motor portion of the Unified Parkinson’s Disease Rating Scale (m-UPDRS). pNN50 was significantly different in patients with and without diabetes mellitus (DM), hypertension (HTN), distal sensory polyneuropathy (DSP), chronic obstructive pulmonary disease (COPD), and kidney disease (p<0.05).

Conclusions:: Resting HRV is positively correlated with reflexive HRV and negatively correlated with age; DM, HTN, DSP, COPD and kidney disease are associated with less heart rate variability and are potential confounders in studies of resting HRV.
Background and Aims:: Objective: To describe a case of Harlequin syndrome in a Movement Disorder Clinic in El Salvador. Background: Harlequin syndrome is a rare dysautonomic disorder characterized by asymmetric facial sweating and flushing in response to heat and exercise.

Methods:: We performed a clinical evaluation and open application of OnabotulinumtoxinA with scheme for the treatment of Harlequin syndrome by a Movement Disorders specialist.

Results:: A 47-year-old female with a 3-year history of episodes of profuse sweating and flushing on the right side of the face triggered by heat, sun exposure and exercise and episodic migraine since childhood (5 episodes per month), with chronic use of over-the-counter medications. Brain MRI was normal. Four cycles of 100 units of OnabotulinumtoxinA were applied to the right hemi face, presenting an 80% improvement in hyperhidrosis and a 90% improvement in migraine episodes and significant reduction in pain medication use. Onset of therapeutic effect was at 7 days, and duration of the maximum therapeutic effect was at 5 months.

Conclusions:: In our patient, OnabotulinumtoxinA was effective in improving unilateral flushing and facial hyperhidrosis and showed a preventive therapeutic effect in episodic migraine.
HIGH THROUGHPUT METHOD TO CLEAN, AND ITERATIVELY FILTER RAW ECG DATA USING OPEN SOURCE SOFTWARE

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Methods:: Using window filters, an iterative process was used to filter each heart rate (HR). Likely artifactual HRs are removed (40 > HR > 180 & HR > 10% mean previous 50 beats). The Hampel filter removes HRs > 4 median absolute deviations (MAD) in a 5-beat window. Smoothing splines were used to interpolation for time analysis measures. We developed and tested the package using patient HRV data (n= 334).

Results:: Following processing with the package <3% of the HR data warranted any manual edits. RMSSD was reduced by ~38% on average and pNN50 by ~9% after filtering. Efficient use of iterative filtering was approximately 6 iterations.

Conclusions:: The open-source “tidyrhrv” package helps to automate the calculation of HRV markers from raw ECG, a process which is otherwise expensive and/or time consuming for large datasets.
Background and Aims:: Patients with primary neurogenic disorders such as pure autonomic failure or multiple system atrophy may present first with cardiocirculatory symptoms such as orthostatic intolerance or fluctuations in heart rate with symptomatic tachycardia. It is therefore clinically important to identify such patients since circulatory manifestations are only one of a series of symptoms resulting from autonomic dysfunction in various organ systems. These patients need a multimodal diagnostic and therapeutic approach and should undergo extensive evaluation in a specialized autonomic nervous system (ANS) outpatient unit.

Methods:: Based on a clinical case presentation, the present review summarizes the diagnostic and therapeutic approach to key cardiovascular symptoms of primary autonomic disorders, and their neurologic work-up in a specialized autonomic function lab.

Results:: The combined neuro and cardio workup in the presented case revealed the diagnosis of PAF with baroreflex failure including OH and supine arterial hypertension, a diminished heart rate variability; quantitative sensibility testing revealed evidence of small fibre neuropathy; and norepinephrine plasma levels were very low. Surprisingly, sudomotor nerve function was normal, despite of clinically severe impairment of sweating.

Conclusions:: Thanks to an increased awareness for symptoms and complaints of autonomic nervous failure and a careful diagnostic workup, even rare neurogenic causes of OI as pure autonomic failure can be detected. The early consideration of specialized neurological and autonomic diagnostics may accelerate the otherwise prolonged and sometimes hopeless search for the origin of OI in patients with multifaced complaints of the ANS.
COMPOSITE AUTONOMIC SYMPTOM SCORE 31: LINGUISTIC VALIDATION FOR RUSSIAN-SPEAKING POPULATION

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Background and Aims:: Reliable assessment of the autonomic symptoms severity is crucial for clinical and academic neurology. Composite autonomic symptom score 31 (COMPASS-31) (Sletten et al. Mayo Clin Proc 2012;87:1196-1201) was translated in many languages. Still, it did not have a validated translation into the Russian language. We aimed to provide linguistic validation of the Russian translation of COMPASS-31.

Methods:: After receiving permission from Dr. Wolfgang Singer and approval from the local ethics committee, we provided appropriate procedure of translation and back translation of COMPASS-31 into Russian. Five hundred thirteen healthy volunteers (166 males, median age 34 years with range 18-69 years) completed COMPASS-31 online. To identify domains of questions and assess their internal consistency, we used exploratory factor analysis with orthogonal rotation and calculated Cronbach alpha-coefficient.

Results:: Factor analysis revealed 9 domains of questions (with the factor loading range 0.477-0.948) that could be combined in originally proposed 6 domains with good internal consistency (Cronbach alpha-coefficient range 0.737-0.931) except for secretomotor domain (Cronbach alpha-coefficient 0.545). Secretomotor domain contained the question regarding sudomotor dysfunction that did not fit any domain but was kept due to its clinical significance as in the original version.

Conclusions:: Our study validated consistency of translated COMPASS-31 for Russian-speaking population that was similar to the original English version of the score. We provided Russian version of COMPASS-31 for clinical and scientific use. Acknowledgement: We are sincerely grateful to Professor Max Hilz (Erlangen, Germany) for the guidance regarding this work.
THE SYSTOLIC TO DIASTOLIC PRESSURE RATIO IN NON-DIPPING ESSENTIAL HYPERTENSION PATIENTS

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Background and Aims:: Nocturnal blood-pressure (BP) decline or dipping is a physiological response in healthy BP-regulation; the lack of this adaptation is frequently observed in patients with essential hypertension (EH) [Chesebro,2020]. Involvement of autonomic dysregulation in EH may result in adrenergic overdrive [Mancia and Grassi,2014; Carthy, 2014]. Heart morphology [Henein, 2011] and systolic to diastolic pressure ratio (SDPR) were previously related to the harmony of the so-called golden ratio (GR=1.618) [Yetkin, 2015]. We aimed here to identify patterns of circadian dysfunction in newly diagnosed patients with EH compared to individuals with normotensive individuals (NIs) by monitoring them with a non-invasive ambulatory blood pressure monitoring (ABPM) system and evaluating their SDPR.

Methods:: Systolic and diastolic BP were monitored for 24 hours (BP lab®, Petr-Telegin) in 14 EH patients and 10 matched NIs, dividing data in awake (day) and sleeping (night) by the actigraph.

Results::

As shown in figure, systolic (p<0.001) and diastolic (p<0.014) pressures were significantly higher in EH patients than NIs in both day and night assessments. In the patient group, SDPR was not significantly different from GR during night and day (p=0.209 and p=0.952). Conversely, in controls, SDPR was significantly lower than GR in day-time (1.52±0.08, p=0.014) but not during night (p=0.695).

Conclusions:: The circadian trend of comparative arterial pressure assessed by SDPR is close to GR in all subjects. However, differently from NIs, patients with EH show a reduced ability to modify their SDPR in day-time (during activities). These findings suggest the importance of monitoring SDPR as a biomarker of autonomic dysfunction.
ZIC-4 ANTIBODIES IN LIMBIC ENCEPHALITIS: A CASE REPORT

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Background and Aims:: Limbic encephalitis (LE) is an inflammatory disease involving the brain’s limbic structures. Typical symptoms include memory deficits, behavioral changes, psychosis, and seizures. Frequently, it is associated with antibodies against the central nervous system (CNS). Serum and cerebrospinal fluid tests for anti-LGI1, GABABR, AMPAR, CASPR2, Hu, Ma2, and GAD must be performed, as positive results might underlie a specific tumor. Zic-4 antibodies are more likely linked to cerebellar dysfunction as paraneoplastic form related to small-cell lung cancer (SCLC). We report a case of LE with isolated Zic-4 antibodies positivity. The latter should be included in the ALE antibodies list.

Methods:: A 66-year-old gentleman is admitted with confusion and acute psychosis. Although his past medical history was unremarkable, his sister reported a 2-months history of behavioral disturbances (spending money and anxiety). Over the following weeks, his condition rapidly declined: short-memory deficits, disorientation, hallucination, aggression, and confabulation occurred. Cerebral spinal fluid analysis showed normal 14-3-3 protein levels, and PCR results were negative for the neurotropic viruses. Cerebral MRI and PET were normal. EEG showed diffuse slow activity without epileptic discharge. HIV, syphilis, borreliosis were negative.

Results:: Zic4 antibodies were found in serum; endovenous immunoglobulin therapy ensued with mild clinical improvement. Unlikely, he got a SarCov2 infection needing CPAP treatment. Cytologic pleural spillage exam (shown on chest CT scan) to investigate malignant cells related to SCLC has not yet been performed.

Conclusions:: Zic-4 antibodies have been mainly associated with cerebellar dysfunction. Our findings suggest that LE symptoms should prompt extensive onconeural antibodies screening among with Zic-4.
CERVICAL DISC HERNIATION OR CERVICAL SPONDYLOSIS MAY CAUSE UNILATERAL OR SEGMENTAL ANHIDROSIS: THE DISTRIBUTION OF ANHIDROSIS DEPENDS ON THE SITE OF SPINAL CORD COMPRESSION

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Background and Aims:: Some patients with unilateral or segmental anhidrosis have cervical disc herniation or cervical spondylosis. We investigated whether cervical myelopathies by these pathemas were involved in those sweating disorders.

Methods:: We analyzed 14 patients aged 37–74 years with unilateral or segmental anhidrosis in the absence of causative abnormalities other than cervical disc herniation or cervical spondylosis. The patients were exposed to 40°C ambient temperature and examined the total sweat distribution (Minor’s method) and distribution of the total skin temperature by infrared thermography, and performed MRI to confirm the lesion.

Results:: MRI revealed the largest protrusion of the intervertebral disc toward the almost anhidrotic side at the midline (paramedian herniation) significantly (89%) in the patients with unilateral anhidrosis, and area 3 mm lateral to the midline (lateral herniation) to segmental anhidrotic side significantly (100%) in the patients with segmental hemianhidrosis. In 80% of the latter patients, disc protrusion was ipsilateral and corresponded to the segment of
Conclusions: Paramedian herniation of the intervertebral disc might induce unilateral anhidrosis, while lateral herniation might induce segmental anhidrosis. The protruded disc near the midline may compress the sulcal artery and cause hemilateral insufficient peripheral perfusion for the sudomotor pathway. Disc protrusion at the lateral site may compress the sympathetic premotor neuron in the dorsolateral funiculus and spare the upper segments synapsing with spinal segmental interneurons and propriospinal neurons.
projecting to the intermediolateral nucleus. It is necessary to identify the difference in the site of spinal cord compression from patients with motor and sensory disturbances as well.
HAS THE TIME COME FOR GASTROINTESTINAL FUNCTIONAL TESTING TO BE INCLUDED AS PART OF AUTONOMIC NERVOUS SYSTEM TESTING?

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Background and Aims:: Individuals with autonomic nervous system (ANS) disorders have a high burden of gastrointestinal symptoms. Unfortunately, many of these individuals are diagnosed with functional gastrointestinal disorders without a comprehensive clinical evaluation or an understanding of the underlying pathophysiological mechanism. The ANS regulates all body systems and is responsible for maintaining homeostasis by coordinating responses to physiological processes and perturbations and is integral in controlling functions of the gastrointestinal system.

Methods:: We performed a retrospective analysis of 85 patients that had undergone both quantitative autonomic testing (HUT, Valsalva, HRV to deep breathing, and quantitative sensory testing) along with gastrointestinal motility testing via wireless motility capsule.

Results:: In this cohort 85.6% had a confirmed ANS disorder diagnosed. Of those with an ANS disorder, 82.2% had dysmotility, 78.1% had a mast cell disorder, and 60.3% had all three. 60.3% had dysmotility involving the stomach (44.5% rapid, 54.5% delayed), 35.6% the small intestine (3.8% rapid, 92.6% delayed), 38.4% the colon (25% rapid, 75% delayed), and 38.4% the whole gut (17.9% rapid, 82.1% delayed). While 28.1% had only one region affected, 53.5% had two or more regions affected.

Conclusions:: Given the critical role of the ANS in controlling gastrointestinal functions, it is not surprising that individuals with ANS disorders have high rates of gastrointestinal dysmotility. Additionally, their symptoms often suggest abnormalities beyond alterations in motility and therefore we propose that comprehensive gastrointestinal function testing should be performed as part of an evaluation for ANS disorders when gastrointestinal symptoms are present.
SYMPTOMATIC GASTROINTESTINAL DYSMOTILITY IN AUTONOMIC NEUROPATHY

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Background and Aims:: Autonomic neuropathy (AN) patients frequently experience multi-systemic symptoms, ranging from cardiovascular, urinary, secretory, and gastrointestinal (GI). Further, there is marked heterogeneity among patients, often limiting the yield of conventional diagnostic evaluations. The aim of this study was to describe our single-institution experience with wireless motility capsule (WMC) testing to quantitatively evaluate segmental dysfunction in AN patients with GI symptoms.

Methods:: We utilized an institutional database to identify cases that presented to the University of Utah with undiagnosed GI and autonomic symptoms (2015-2019; n=102). Inclusion criteria: AN diagnosis based on autonomic testing. Of the initial cohort, 27 subjects met inclusion criteria. WMC results were analyzed to identify abnormalities in gastric emptying and small bowel/colonic/global transit times.

Results:: Subjects were predominately female (25/29); aged 17-62 years (median 29). Mean COMPASS-31 score was 54.4, with a mean GI domain score of 15.6. Overall, 25/29 subjects had dysmotility in at least one segment of the GI tract, with a mean of 2.0 segments affected. Of the 14/27 with one or more slow segments on WMC, 13 reported symptoms of constipation, while all of those with one or more rapid segments (8/8) reported symptoms of diarrhea. Of subjects with abnormal sudomotor function, 11/20 showed corresponding anatomical segmental dysfunction in the GI tract on WMC testing.

Conclusions:: In this cohort of AN patients with prominent undiagnosed GI symptoms, 86% had abnormal WMC testing. These findings establish GI dysmotility as a quantifiable feature of AN with GI symptoms, and merit future studies to evaluate underlying pathophysiology.
SEASONAL VARIATION OF BLOOD PRESSURE AND ORTHOSTATIC INTOLERANCE IN PARKINSON'S DISEASE

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Background and Aims:: Patients with Parkinson’s disease (PD) have autonomic dysfunction, for example, orthostatic hypotension (OH). In general, resting blood pressure has seasonal variation and OH may become worsen in summer and ameliorated in winter. It has not yet been studied whether orthostatic intolerance has seasonal changes and it influences on seasonal variation of resting blood pressure in PD. The purpose of this study is to elucidate how orthostatic intolerance in PD is influenced by climatic differences.

Methods:: Subjects were 54 (29 men and 25 women) PD patients with age of 76 ± 6 yrs, disease duration of 4.3 ± 2.6 yrs, and Hoehn-Yahr’s stage of 3.0 ± 0.6 (mean ± SD). Once at a season (spring: Mar.-May, summer: June-Aug., autumn: Sept.-Nov., winter: Dec.-Feb.) in a year, they were asked to visit the outpatient clinic, where they were required to sit on chair for 5 min, and then to stand-up actively within 5 s. The intermittent systolic blood pressure (SBP), diastolic blood pressure (DBP) were measured.

Results:: The resting SBP and DBP were higher in winter than in summer. The SBP decreased by standing in all seasons. The DBP decreased by standing only in summer and the ΔDBP was larger in summer than in other seasons. The ΔSBP and ΔDBP were not correlated the maximum-minimum difference (MMD) of SBP and DBP.

Conclusions:: Seasonal changes in sympathetic outflow to the periphery could be responsible for this orthostatic intolerance in summer, but it could not influence seasonal variation of resting blood pressure in PD.
SENSORY CHANGES IN POSTURAL TACHYCARDIA SYNDROME COMPARED TO CHRONIC MIGRAINE

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Background and Aims:: Postural tachycardia syndrome (PoTS) and migraine frequently present together in clinical practice. Up to 90% of PoTS patients report headaches of some kind, with migrainous headaches as the most widely recognized primary headache in this cohort. Given this comorbidity, pathophysiological interaction is possible, which could identify key features of disease pathophysiology and targeted treatment interventions. We hypothesized that migrainous and non-migrainous PoTS subjects would show features of central sensitization, including allodynia and photophobia.

Methods:: Eighty patients (30 PoTS, 30 chronic migraine [CM], and 20 non-headache healthy controls [NH]) were evaluated via tilt table testing, sensory sensitivity thresholds, and questionnaire to evaluate headache burden and associated symptoms. Sensory thresholds and clinical characteristics were compared across groups, including PoTS sub-group analysis based on headache phenotype.

Results:: Sensory sensitivity thresholds were significantly lower and symptom scores were higher in PoTS and CM groups compared to controls. Interestingly, however, the expression patterns differed between PoTS and CM, with reduced pain thresholds in the forearm expressed most prominently in PoTS subjects, compared to both periorbital and forearm lower thresholds in CM. Light sensitivity thresholds were significantly lower in PoTS than either CM or NH.

Conclusions:: These distinguishing aspects of PoTS disease burden reveal an underappreciated aspect of this syndrome, and suggest network sensitization similar to, but separable from, that of migraine. The finding of non-trigeminally-mediated sensitization in PoTS supports prior reports of central sensitization, while providing further evidence that PoTS might be considered a multisensory gain disorder, with distinct physiological manifestations.
Background and Aims:: Meningitis is the inflammation of tissues which covers brain & spinal cord. Thus lactyl stearate coupled liposomes bearing rifampicin (highly lipophilic) is used for effective management of meningitis. Brain drug targeting brings a healthy skepticism to the study of the BBB, which is the most frustrating obstacle for pharmacologists wishing to find treatments for brain disorders.

Methods:: Synthesized Lactyl stearate was used to prepare liposomes bearing rifampicin by Lipid cast film method. Formulations were characterized for vesicle shape by Transmission Electron Microscopy(TEM), vesicle size, drug entrapment efficiency, in-vitro drug release. The in-vivo studies the drug distribution in various organs and blood of albino rats was assessed after I.V. administration. The quantitative uptake of the formulations by the brain in albino rats was assessed by fluorescent microscopy.

Results:: The % encapsulation efficiency was 41% & 34% in uncoupled & coupled liposomes. Brain uptake was increased about 2-3 times in case of uncoupled liposomes and plain drug. Accumulation was increased about 6-8 times with coupled liposomes in comparison to uncoupled and about 10-12 times higher compared to drug solution.

Conclusions:: Fluorescence study indicates that the preparation is crossing basal carotid system & accessing the nervous system. This delivery system not only increased the brain uptake of the drug but it also reduces the administered dose and toxic effect of the drug. Thus, Lactyl stearate coupled liposomes effectively delivers the drug to the brain and has great potential for brain targeting.
PUPIL INVOLVEMENT IN PATIENTS WITH DIABETES-ASSOCIATED OCULOMOTOR NERVE PALSY

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Background and Aims:: Introduction: Diabetics are predisposed to acute mononeuropathies, including oculomotor nerves. It was noted that pupil involvement in diabetes occurs more often than has been previously recognized.

Methods:: A 55-year-old man with a medical history of poorly controlled diabetes and hypertension presented with a non-fluctuating droopy eyelid with diplopia. Ophthalmo logical exam revealed palsy of the right oculomotor nerve with bilateral mydriasis and an abolished light reflex. Dilated fundus exam showed non-proliferative diabetic retinopathy. Neurological exam revealed an associated proprioceptive dysfunction. Cerebral MRI and MRA showed no pathological findings, no aneurysmal compression of the oculomotor nerve was found. The examination of cerebrospinal fluid was normal. Laboratory tests including thyroid hormones, immunologic and infectious testing were normal. ENMG showed length dependent neuropathy. One week later, mydriasis and ptosis regressed. Light reflex became normal.

Results:: Pupillary involvement in diabetes-associated oculomotor nerve palsy occurs in about 1/4th of all cases. Dysfunction of the parasympathetic nervous system causes relative mydriasis and diminished constriction to light. This condition can explain the pupillary involvement in diabetes. Certain pupil characteristics like an incomplete pupillary involvement and anisocoria < 2 mm may help to distinguish diabetic from aneurysmal (compressive) injury of the oculomotor nerve. Imaging should be considered when patients present with additional cranial nerve palsy or neurological abnormalities or where pupil shows characteristics of a compressive lesion.

Conclusions:: Abnormal pupillary dynamics in diabetes is suggestive of an autonomic neuropathy. It progresses with the severity of retinopathy. Mydriasis is quite rare but imaging should be considered in order to rule out other differential diagnosis.
Background and Aims:: Paediatric acquired demyelinating syndromes (ADS) represent a group of clinical conditions caused by inflammatory processes in the central nervous system (CNS). An early differential diagnosis between a monophasic and a chronic or relapsing form is crucial. Main treatments available for acute attacks are steroids and intravenous immunoglobulins (IVIg), while more recently there is increasing evidence of efficacy of disease-modifying therapies (DMTs) for chronic forms, including periodic cycle of IVIg, showing that an early treatment is fundamental to avoid disability accrual.

Methods:: We describe the case of a 10-year-old girl with a diagnosis of autism spectrum disorder presenting with three attacks of encephalopathy, seizures and focal neurological signs. Brain MRI, performed at different times, showed bilateral, cortical-subcortical, supra-infratentorial demyelinating lesions, compatible with multiphasic acute disseminated encephalomyelitis (ADEM). Anti-MOG antibodies were found in the serum, while anti-AQP4 were negative. The patient was treated with steroids and monthly cycles of IVIg with good clinical and radiological response and no more relapses; however, serum anti-MOG antibodies positivity persisted for more than 6 months.

Results:: The features of disease onset, the clinical and radiological progression of the patient, and the response to steroids and IVIg cycles suggest a form of ADS of multiphasic ADEM-like presentation with persistent anti-MOG antibodies positivity, compatible with a MOG Antibody Disease (MOGAD).

Conclusions:: The unusual case suggests the need of a multidisciplinary approach (neurologists, neuropediatricians, neuro-radiologists) and a strict clinical and radiological follow up of these patients. We here provide a flow-chart of clinical management by reviewing existing literature on ADS in pediatric
DYGGVE-MELCHIOR-CLAUSEN SYNDROME: A MUCOPOLYSACCHARIDOSIS MIMIC

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Background and Aims:: Dyggve–Melchior–Clausen (DMC) syndrome is a rare, autosomal recessive, progressive Spondylo-epi-metaphyseal dysplasia caused by mutations in Dym gene mapped on chromosome 18q12-12. Due to significant differences in prognosis and treatment, it is important to ascertain the diagnosis in such cases.

Methods:: We present a 9-year old child who was brought with complaints of intellectual disability and severe bony deformities. Child was born out of consanguineous marriage at full term. On examination, child had short stature and microcephaly along with coarse facies, short forehead, prominent ears, thick lips and macrognathia. A short-neck and deformed chest was present with pectus carinatum and flaring of costal margins. Rhizomelic shortening of upper limbs was noted. Genu valgum; with fixed flexion deformity in both lower limbs. Neurological assessment revealed profound mental retardation with a social age of 11.3 months according to VSMS (Vineland Social Maturity Scale). MRI brain showed thinning of corpus callosum. Considering a possibility of Mucopolysaccharodosis, urinary glycosaminoglycan screen was done which was negative. Radiography revealed widening of anterior ends of ribs, dorsolumbar spine showed evidence of platyspondyly with double hump deformity, hypoplastic ilium with widened acetabulum and lacy iliac crest were spotted on radiographs of pelvis. Femoral epiphyseal flattening and compression with metaphyseal splaying were noted.(Figure 1-3)

Results:: Hence, in view of mental retardation with radiological features and absence of urinary glycosaminoglycans with a history of consanguinity consistent with autosomal recessive nature of the disease, a diagnosis of DMC syndrome was established for this child. Gene studies could not be done due to non-affordability

Conclusions:: Rates of survival with DMC syndrome are better however the quality of life is limited by bony significant bony deformities.
ADRENOCORTICOTROPIC HORMONE INDUCED STATUS DYSTONICUS: CAUTION ADVISED

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Background and Aims:: Dystonia is a movement disorder characterized by involuntary sustained or intermittent muscle contraction causing repetitive twisting movements and abnormal postures. The localization of dystonia is dysfunctional interactions of basal ganglia, cerebellum, thalamus, cerebral cortex and brainstem. Status dystonicus, or dystonic storm, is a life threatening emergency marked by development of increasingly frequent or continuous severe episodes of generalized dystonic spasms. The etiology of status dystonicus has not been clearly. We hereby present a case report of a child with WS who went on to develop status dystonicus following intramuscular ACTH injection.

Methods:: Eleven month old male child presented with complaints of flexor spasms for 2 months. There was history of birth asphyxia followed by mechanical ventilation for a period of 5 days. Child had global developmental delay with MRI brain showing sequelae of perinatal hypoxic insult. The diagnosis of WS was confirmed by EEG which showed hypsarrhythmias. Intramuscular ACTH was added and oral trihexyphenidyl was started for dystonia. On day 7 of ACTH, child developed frequent ophisthotonic posturing.

Results:: Management protocol for grade 4 status dystonicus was initiated and child was shifted to Pediatric Intensive Care Unit. The dystonias gradually responded over the next week and child was slowly weaned off sedatives.

Conclusions:: Administration of N terminal of ACTH in rat locus coeruleus has been shown to produce human dystonia like movement and abnormal posturing. Effectiveness of anticholinergics against dystonia has been attributed to suppression of ACTH released caused by them.
INVESTIGATION OF THE OCCUPATIONAL PERFORMANCE OF THE CHILDREN WITH NEURODEVELOPMENTAL DISABILITIES DURING THE COVID-19 PANDEMIC

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Background and Aims:: All individuals, including children, had difficulties in fulfilling their roles, and children with neurodevelopmental disorders faced many difficulties in attending therapies since the pandemic began. This study was aimed to investigate the change in the occupational performance of the children with neurodevelopmental disabilities during the Covid-19 pandemic.

Methods:: Children aged 6-12 years with neurodevelopmental disorders and their caregivers (n=40) were included in the study from Hacettepe University Faculty of Health Sciences, Department of Occupational Therapy, pediatric unit. After the pandemic, the children with neurodevelopmental disabilities who came to the clinic for occupational therapy were diluted and some of them continued face-to-face therapies, while others continued their therapy with the telerehabilitation method. The Canadian Occupational Performance Measure (COPM) was applied to caregivers twice, in March 2020 and March 2021. Wilcoxon test was used for analysis.

Results:: Even though the change in occupational performance was clinically significant in children who received therapy face-to-face, but there was no statistically significant change in occupational performances with either method (p>0.05).

Conclusions:: According to the results of the study, there was no significant change found in the occupational performance (performance and satisfaction) scores during the pandemic. The reason may have been participants’ desires and situations to continue the therapies were affected negatively and the level of anxiety of families was increased.
THE EFFECT OF OCCUPATIONAL THERAPY HOME INTERVENTION ON ORAL SENSORY PROCESSING AND NUTRITION PROBLEMS IN CHILDREN WITH ORAL HYPERSENSITIVE DOWN SYNDROME

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Background and Aims:: This study aimed to investigate the effect of home program on oral sensory processing and nutritional difficulties in children with oral hypersensitive Down Syndrome.

Methods:: The study included a total of 36 children; 18 oral hypersensitive Down Syndrome between the age 3-8 and 18 healthy children. Oral sensory processing of these children were determined by Dunn Sensory Profile (DSP), nutritional difficulties were determined by Screening Tool of Feeding Problems (STEP). All of the children underwent routine occupational therapy (sensory integration) and 10 of them were provided an extra home program on oral sensory processing. The home program was controlled with a schedule. Children were evaluated twice before and after the intervention.

Results:: When the participants were examined, oral sensory processing and nutritional difficulties were observed. Significant improvements were found in the DSP’s oral sensory process subtest and STEP scores after occupational therapy and home program group (p <0.05).

Conclusions:: The benefits of sensory integration-based occupational therapy interventions in children with Down syndrome are known. In addition, these children may have oral sensory processing and nutritional difficulties. It was observed that occupational therapy and home programs for this purpose reduced significantly oral sensory processing and nutrition problems. Therefore, it is important to support occupational therapy intervention programs with home programs in children with down syndrome who affected by oral sensory processing.
THE EFFECT OF BIMANUEL TRAINING ON OCCUPATIONAL PERFORMANCES IN A CHILD WITH ISOLATED MIRROR MOVEMENT DISORDER: A CASE STUDY

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Background and Aims:: Mirror movements disorders (MMD) are defined as involuntary movements of the contralateral homologous extremities during voluntary movements of one side. Mirror movements were reported with many developmental defects, diseases, or autosomal dominant and autosomal recessive inherited and no certain reason displayed types. The aim of this study was to investigate the effect of occupational therapy on occupational performance in a child with MMD.

Methods:: A child aged 15 years with MMD was admitted to the study. To evaluate occupational performance, the Canadian Occupational Performance Measure (COPM) was applied. Occupations that are considered to be important for the child are determined as written work, manipulation movement, eating and drinking, and functional communication respectively. Activities to improve bimanual and social skills for the occupational therapy program seemed appropriate. During the intervention, selected activities were conducted for 12 weeks a day per week for 55 minutes each day.

Results:: As a result of the intervention, the COPM performance score increased from 2 to 6 and the COPM satisfaction score of these activities increased from 1,75 to 5,75. It was seen that occupational therapy including bimanual and social skill activities was effective in increasing the occupational performance of the child.

Conclusions:: The research evidence supports that occupational therapy improves occupational performance and satisfaction in everyday life for children with MMD. Because the knowledge of the clinical aspects of these disorders is insufficient. It is therefore important to understand the impact of occupational therapy and to ensure its quality and accessibility.
ATYPICAL AURAS IN PEDIATRIC MIGRAINE: CLINICAL SERIES AND PATHOPHYSIOLOGICAL CORRELATIONS.

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Background and Aims:: Aura is one of the most important symptoms of migraine and “Cortical Spreading Depression (CSD)” has been suggested as the most plausible underlying pathophysiological mechanism. However, recent reports raised doubt against the concept that CSD could account for all presentations of migraine aura. Here, we show a series of atypical paediatric aura hardly explainable by the CSD principles, suggesting partly different pathophysiological mechanisms.

Methods:: We selected retrospectively all clinical records that presented migraines aura that can be considered as atypical on the basis of the following criteria: 1)the spreading wave appears to be not related to the CSD model; 2)the chronological sequence and homunculus are not respected by the sequence and characters of aura symptoms; 3)time intervals between symptoms onset not justified by CSD theory; 4)atypical clinical symptoms not accountable by CSD; 5)atypical correlation with pain onset and pain side.

Results:: We collected 15 cases (5 M/10 F, range age 9-16ys). All subjects underwent EEG and BrainMRI. The subjects were subdivided according to the criteria(see above) why their aura were found to be atypical: Four subjects satisfied the criterion 1; Five the second; Five the third; Five the fourth; one the criterion 5; some children satisfied more than one criterion.

Conclusions:: Our series shows that the current CSD theory cannot fully explain the modalities of the aura presentation in some subjects. Therefore, some aspects need further investigation and reassessment, on the basis of clinical practice. Furthermore, we underline how accurate exploration of the migrainous aura can provide useful insight on pathophysiological aspects.
NODDI DISCLOSES EARLY CHANGES IN THE NORMAL APPEARING WHITE MATTER IN PAEDIATRIC MULTIPLE SCLEROSIS.

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Background and Aims:: Paediatric-onset multiple sclerosis (PedMS) is characterized by high degree of brain inflammation and rapid accumulation of white and grey matter damage. Abnormalities in the normal appearing white matter (NAWM) and their clinical relevance in PedMS were investigated by Neurite Orientation Dispersion and Density Imaging (NODDI).

Methods:: Eighteen PedMS and 10 age- and sex-matched healthy controls (HC) underwent a 3T brain MRI; clinical disability was assessed through the Expanded Disability Status Scale (EDSS). Individual maps of intracellular volume fraction (ICVF), extracellular volume fraction (ECVF) and orientation dispersion index (ODI) were obtained. Between-group differences in diffusion tensor/NODDI measures were investigated in the corpus callosum (CC), cortico-spinal tract (CST) and posterior thalamic radiation (PTR). Their association with clinical scores were also evaluated.

Results:: Compared to HC, pedMS showed significantly lower ICVF and higher ECVF values in all the WM tracts investigated (p≤0.038). In the PTR, patients showed lower FA (p=0.006) and higher MD (p=0.029). Lower FA and ICVF values in the CC NAWM were associated with a higher CC LV (r=-0.592, p=0.006; r=-0.582, p=0.007, respectively), whereas higher CC NAWM MD and ECVF were associated with higher CC LV (r=0.575, p=0.008; r=0.657, p=0.002). EDSS score positively associated with CC and PTR LV (r=0.471, p=0.049 and r=0.556, p=0.017, respectively), CC NAWM MD (r=0.580, p=0.012) and ODI (r=0.613, p=0.007) and PTR NAWM ODI (r=0.574, p=0.013)

Conclusions:: NODDI disclosed significant microstructural changes in the NAWM of pedMS. Our findings further provide in vivo evidence supporting the hypothesis that inflammatory-triggered neurodegeneration affects MS brain since the biological onset of the disease.
SURVEY OF BRAZILIAN CHILDREN WITH CEREBRAL PALSY: A RETROSPECTIVE STUDY

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Background and Aims:: Cerebral palsy (CP) is known worldwide as the most prevalent cause of motor disability during childhood. In Brazil, there are no epidemiological studies of this population. Thus, with this study we aim to verify the epidemiological data of children and adolescents with CP, followed up at the neuropediatrics outpatient clinic of Brasília University Hospital.

Methods:: This research was approved by the Ethics Research Committee (34383220.9.0000.5558). All medical records of patients attended in the neuropediatrics clinic between 2000 and 2020 were analyzed retrospectively to verify: number of children with CP; clinical type; etiology; associated comorbidities; use of medications. Analysis of the data was attained by descriptive statistics.

Results:: Were analyzed 1199 medical records, of which 119 (9.9%) were of children with CP. The clinical types identified were: 115 (96.6%) spastic, 2 (1.6%) ataxic, 2 (1.6%) dyskinetic. Malformations of the central nervous system (28.6%), hypoxic-ischemic encephalopathy (26.8%), neurogenetic syndromes (10.9%), prematurity (7.5%) represented the main etiologies. Among children with CP, 59.6% had epilepsy, 26.8% showed neurodevelopmental disorders and 12.6% presented endocrinopathies. Regarding medications, approximately 40% of children used antiepileptic, 8.4% psychostimulants and 8.4% baclofen.

Conclusions:: The prevalence data obtained on clinical types and etiologies do not correspond to those observed in the world literature. This discordance may be justified due to subdiagnosis of CP in Brazil and the lack of data in the medical records. More studies are needed to identify the profile of Brazilian children with CP in order to adapt the therapeutic planning to this population.
SPEECH DYSORDERS IN CHILDREN WITH COGNITIVE EPILEPTIFORM DISINTEGRATION AGED 2-10

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Background and Aims:: Cognitive epileptiform disintegration (CED) is a symptomatic complex of acquired cognitive disorders in children associated with severe epileptiform activity on the EEG in the absence of epileptic seizures. It is one of the reasons for developmental dysphasia, the cases of which rapidly increase. The aim of the study is to reveal the structure of speech disorders in children with CED.

Methods:: From 2016 till March 2021 we observed 112 children aged 2-10 with CED (76 preschoolers, 36 from primary school). All children passed through neurological examination and video-EEG-monitoring with sleep deprivation. Speech was assessed with reliance on the principles worked out by T.V.Akhutina et al., by 25 specific subtests created at the Laboratory of Clinical linguistics (Kazan Federal University).

Results:: In 97 children (97: 86.6%) we registered speech disorders: total absence of expressive and impressive speech (19: 16.9%); impressive speech disorders (28: 25%); general speech retardation (43: 26.7%); echolalia (31: 27.7%); logorrhea (42: 37.5%); non-communicative speech (23: 20.5%); delayed answers to the questions (16: 14.2%); dyslexia, dysgraphia (28 from 36 schoolchildren/77.7%). 84.5% of children with speech impairment had autism spectrum disorders (ASD) (non-stable response to the name, stereotype behavior, emotional deficit, etc.). In 63.5% there were attention deficit and hyperactivity disorders (ADHD).

Conclusions:: The analysis of speech development in children with CED shows that impressive speech disorders are primary in relation to other types. They are closely connected with ASD and ADHD. This work was supported by the Program of Strategic Academic Leadership of Kazan Federal University.
EPIDEMIOLOGICAL, CLINICAL AND PARA CLINICAL CHARACTERISTICS OF NEURODEGENERATION WITH BRAIN IRON ACCUMULATION IN CHILDHOOD

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Background and Aims:: Neurodegeneration with brain iron accumulation (NBIA) represents a clinically and genetically heterogeneous group of disorders. The aim of our study is to describe epidemiological, clinical, and paraclinical characteristics of NBIA in children.

Methods:: We conducted a descriptive, retrospective study over 14 years, including patients followed up for NBIA in the department of Child and Adolescent Neurology in National Institute Mongi Ben Hmida of Neurology of Tunis.

Results:: Thirty-nine patients were followed up for NBIA. The sex-ratio M/F was 1.29. Six patients were followed for genetically confirmed Pantothenate-kinase-associated neurodegeneration. The mean age of onset was 4.4 years. Main initial clinical feature was dystonia. MRI revealed the eye of the tiger sign in all cases. Thirty-three patients were diagnosed infantile-neuroaxonal-dystrophy (INAD). The mean age of onset was 14 months. All patients had psychomotor regression, hypotonia, and spastic tetraparesis. MRI showed cerebellar atrophy in all cases. PLA2G6 mutations were found in 17 patients. Two siblings (girl: 16 years, boy: 7 years) were followed for a genetically confirmed Mitochondrial-membrane-protein-associated neurodegeneration (MPAN). They presented with spastic paraparesis and cognitive impairments. MRI showed hypointense signal in the globi pallidi with a T2 hypointense signal in the sub thalamic nuclei in the girl’s case. A 7-year-old boy had a Neuroferritinopathy. He presented with parkinsonism. MRI showed T2 hyperintense signal in the pallidi and the dentates.

Conclusions:: The main characteristics of our study is the predominance of INAD among other NBIA and the possible involvm ent of the subthalamic nuclei MPAN. Larger studies could provide more information about this disease.
NEUROLOGICAL AND NEUROPSYCHOLOGICAL EXAMINATION OF CHILDREN WITH ALALI

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Background and Aims:: Sensorimotor alalia (SMA) is a disorder of impressive and expressive speech development without the previous period of normal speech according to ICD-10. Neurological/neuropsychological examination of children with SMA helps conduct speech habilitation. The aim of the study is to determine the neurological and neuropsychological specificity in children with SMA.

Methods:: The research included 94 patients aged 3.1–8.0 with SMA, 72 boys (76.6%) and 22 girls (23.4%). Inclusion criterion: SMA. Exclusion criteria: traumatic brain injury, epilepsy, epileptiform cognitive disintegration, neuroinfection, aphasia, hearing impairment, mental retardation, autism spectrum disorders. All children passed neurological examination, neuropsychological (methodology of T.V. Akhutina et al.) and speech assessment (tests worked out at the Laboratory of clinical linguistics (KFU).

Results:: 83(88.2%) patients had microfocal neurological symptoms: diffuse muscle hypotension in 69/94(73.4%), motor problems – 42/94(44.6%), coordination – 36/94(38.3%), pyramidal symptomatology in the lower limbs – 22/94(23.4%), gait with internal rotation of stop socks – 12/94(12.8%), non-progressive moderate hydrocephalic syndrome – 9/94(9.5%), apraxia elements – 8/94(8.5%), unstable convergent strabismus – 3/94(3.1%), hypersalivation 3/94(3.1%), pseudobulbar syndrome – 2/94(2.1%), eye slits asymmetry – 1/94(1%). 83(88.2%) patients had neuropsychological specificity: deficiency of executive functions – 44/94 (46.8%), attention deficit – 43/94(45.7%), echolalia – 36/94(38.3%), kinesthetic processing deficiency – 22/94(23%), visual-spatial gnosis deficiency – 18/94(19.1%), lack of energy supply to the brain –13/94 (13.9%).

Conclusions:: The majority of children with SMA had deficiency of executive functions, attention deficit and a tendency to echolalia, diffuse neurological micro-focal symptoms, and frontal-cerebellar symptoms. This work was supported by the Program of Strategic Academic Leadership of Kazan Federal University.
Background and Aims:: Deficiency of adenosine deaminase type 2 (DADA2) is a rare monogenic vasculitis syndrome caused by mutations in the ADA2 gene that encodes the adenosine deaminase 2 (ADA2) protein. It is an autosomal recessive disease characterised by a large phenotypic variability due to the many organs that can be affected. Ischemic and/or hemorrhagic stroke could be a manifestation of the disease. We described a case of ischemic stroke as presentation of DADA2.

Methods:: Case report and literature review.

Results:: A nine-year-old girl experienced wake-up diplopia. Headache or other symptoms were not complained. History of recent minor head trauma was reported. No fever or recent infections were present. Family history was negative. Neurological examination showed oculomotor deficit in left eye with diplopia, no other deficits were observed. General examination was normal, and no other signs of vasculopathy were detected. Brain RM showed small acute left paramedian mesencephalic and right thalamic ischemic lesions; moreover, a chronic right posterior thalamic ischemic lesion was observed. MR angiography documented a thin vertebro-basilar artery system without occlusions. Conventional cerebral angiography was normal. Laboratory investigations showed a slight CRP increase. Viral screening, and cerebrospinal fluid examination were normal. Prothrombotic disorders were excluded. Cardiological investigations showed small patent foramen ovale. Genetic workup showed mutations in the ADA2 gene. We concluded for ischemic lacunar stroke as first manifestation of DADA 2.

Conclusions:: Early etiological diagnosis of ischemic stroke in pediatric population is difficult. It should always include a complete diagnostic workup to identify rare disease as DADA 2, and provide appropriate therapy.
EFFICACY AND SECURITY OF ONASEMNogene ABEPARVOVEC-XIOI IN SPINAL MUSCULAR ATROPHY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims:: Onasemnogene abeparvovec-xioi is a gene therapy approved by FDA in 2019; however, the drug profile is not fully known. We aimed to evaluate efficacy and security of Onasemnogene abeparvovec-xioi in patients with type 1 spinal muscular atrophy (SMA).

Methods:: We conducted a literature search in databases PubMed, SCOPUS and the Cochrane library, until January 2020. We performed a meta-analysis using the univariate model of random effects, and heterogeneity was evaluated using I2. Funnel plots, and Egger’s test were used to evaluate publication bias. The certainty of evidence was assessed with the GRADE system.

Results:: We selected 3 studies with a total of 137 patients. We found that 87.82% (95%CI 72.92-102.71) achieved the ability of swallowing and 83.11% (95%CI 68.67-97.58) attained the ability of sitting with very low certainty of evidence. The motor function, measured by the CHOP INTEND score at three months, showed an increase of 7 points ± 8.72 SD in one study and an increase of 15.4 points in another study with low certainty of evidence. Adverse effects reported were elevated transaminases with a frequency of 67.44% (95%CI 35.56-99.31), fever/pyrexia with 45.42%(95%CI 28.47-62.37) and serious adverse effects (transaminase elevation> 10 times normal, vomiting) with 11.83% (95%CI 5.88-17.77), all of them with very low certainty of evidence.

Conclusions:: With very low certainty, Onasemnogene abeparvovec-xioi improves the achievement of sitting and swallowing abilities with few serious gastrointestinal and systemic adverse effects in patients with type 1 SMA.
SCREENING FOR NEURODEVELOPMENTAL DISORDERS AMONG CHILDREN WITH UNTREATED EPILEPSY IN NORTHERN NIGERIA

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Background and Aims:: Little is known of the frequency of neurodevelopmental disorders among children with untreated epilepsy in sub-Saharan Africa. The "Bridging the Childhood Epilepsy Treatment Gap in Africa (BRIDGE)" project identified children with untreated epilepsy for a cluster non-inferiority randomized clinical trial of task-shifted care, and screened these children for neurodevelopmental disorders.

Methods:: A previously validated Hausa language version of a 23-question screening questionnaire (23Q) for autism spectrum disorder (ASD), cerebral palsy (CP), intellectual disability (ID), and hearing impairment (HI) was administered to parents of children with previously untreated epilepsy enrolled in the BRIDGE project. The 23Q was administered by epilepsy-trained CHWs, trained in the 23Q as part of their preparation for the BRIDGE project. Data were entered directly into REDCap® and uploaded to the BRIDGE Data Coordinating Center for analysis.

Results:: Among children who were eligible for screening, 31% (459 of 1482) screened positive for possible CP, 16.7% (248 of 1489) screened positive for possible HI. 48% (707 of 1474) screened positive for possible ID, and 28.5% (403 of 1412) screened positive for possible ASD.

Conclusions:: The percentage of children with epilepsy who screened positive for ID, ASD, HI and CP was significantly higher among children with untreated epilepsy in northern Nigeria than expected based upon studies of neurodevelopmental disabilities among children with epilepsy from the US and Europe. Detailed neurodevelopmental assessments are underway among children who screened positive for these disabilities in the BRIDGE project. More research on neurodevelopmental co-morbidities among untreated children with epilepsy in sub-Saharan Africa is needed.
CORRELATION OF COGNITIVE IMPAIRMENTS WITH SCHOOL PERFORMANCE DEPENDING ON THE FORM OF CEREBRAL PALSY.

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Background and Aims:: Purpose of the study: determination of the severity of cognitive impairments depending on the form of the cerebral palsy in order to determine their further education.

Methods:: 25 children with various forms of cerebral palsy of preschool age were examined. Analysis of cognitive functions using special scales (Wechsler's scale of cognitive function adapted for children from 4.5 to 6.5 years old).

Results:: A study of cognitive functions according to the Wechsler scale adapted for childhood was carried out in 25 patients with cerebral palsy of the non-dominant hemisphere (6 patients with spastic diplegia, 5 with double hemiplegia, 5 with a hemiparetic form, 5 with hyperkinetic, 4 - with atonic-astatic) at the age of 4.5 to 7 years on the basis of the Cerebral Palsy Center and the Children's Clinical Hospital #4. It was found that intellectual development close to normal was observed in 60% of patients with hemiparetic form, in 33% with spastic diplegia, 40% with hyperkinetic form, 25% with atonic-astatic form and in 20% of patients with double hemiplegia. Mental retardation was observed in 50% of children with atonic-astatic form, 40% with hemiparetic, 16.7% with spastic diplegia, 20% with hyperkinetic form of the cerebral palsy, 20% with double hemiplegia.

Conclusions:: • Children with spastic diplegia and hemiparetic form of the disease with lesions of the non-dominant hemisphere were recommended to study in general education schools. • Children with atonic-astatic and hyperkinetic form of the disease - in specialized schools. • Children with double hemiplegia – home education.
CLINICAL AND PARA CLINICAL FEATURES AND THE NATURE OF THE COURSE OF EPILEPTIC ENCEPHALOPATHY IN PRESCHOOL CHILDREN

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Background and Aims:: Currently, some researchers consider interictal epileptic psychoses as a manifestation of epileptic encephalopathy (EE).

Methods:: This study was based on the data of examination of 30 children with a diagnosis of EE at the age of 3 to 7 years. In this work, we used general clinical, neurological and instrumental research methods (EEG).

Results:: According to the data obtained, we found that 8 children (26.6%) with EE were diagnosed with Lennox-Gastaut syndrome, Landau-Kleffner syndrome - in 3 (10%) and in 2 (6.7%) West syndrome. All these children were classified as type I EE. Tonic seizures were observed in 11 children (36.67%), among them short-term seizures were recorded in 8 children, which lasted for several seconds. Atypical absence seizures were observed in 5 patients (16.7%), had a relatively gradual onset and end, in contrast to the sudden nature of typical absences. Atonic seizures were observed in 7 children (23.3%) and were characterized by a sudden and significant loss of postural tone with the involvement of the whole body or only the head muscles. Myoclonic seizures were recorded in 4 patients (13.3%) (nodding, pecking, flinching). Polymorphism of epileptic seizures was observed among 23.3% (7 children) of patients. When analyzing the neurological status, it was found that children with type 1 EE are characterized by micro-focal neurological symptoms in the form of: disorders of the cranial nerves, pyramidal insufficiency, transient coordination disorders.

Conclusions:: Thus, type I EE is characterized by micro-focal neurological disorders with progressive disorders of the cognitive sphere, intelligence, speech and other cerebral functions.
NEUROCOGNITIVE DEFICITS IN SICKLE CELL DISEASE

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Background and Aims:: The neurological burden of sickle cell disease remains poorly documented. The current study was aimed at assessing neurocognitive functions in Congolese children with sickle cell disease.

Methods:: Neurocognitive assessments using the Kaufman Assessment Battery for Children, 2nd edition (KABC-II) for cognition testing and the Bruininks/Oseretsky Test, 2nd Edition (BOT-2) for motor proficiency were performed in 189 children (102 boys vs. 87 girls, 9.8 ± 2.5 years of age, overall; 129 homozygous (SS), 38 heterozygous (AS), and 22 non-carriers (AA). Predictors of neurocognitive performance were determined using general linear models at the significance level p˂0.05 (STATA, version 12.1.)

Results:: Overall, sickle cell disease was associated with poor motor performance (p = 0.001). Mental processing and motor proficiency were negatively with advanced age [beta (CI): -0.093 (-0.150; -0.037), p = 0.001] and [beta (CI): -0.131 (-0.174; -0.088), p <0.001], respectively. Mental processing was also positively associated with socioeconomic status (SES) [beta (CI) = 0.228 (0.139; 0.317), p<0.001]. Children on hydroxyurea had higher performance scores at motor and cognitive testing at simultaneous and sequential processing, learning, planning, and delayed recognition (p <0.05).

Conclusions:: Scaling up treatment with hydroxyurea and SES- and gender-focused rehabilitation strategies may improve neurocognitive outcomes in children with sickle cell disease.
CASE REPORT: HEREDITARY SPASTIC PARAPLEGIA WITH THIN CORPUS CALLOSUM

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Background and Aims:: Hereditary spastic paraplegias (HSPs) are a group of inherited neurodegenerative disorders with clinical varieties depending on the genetic profile. Since 1981 it was established the clinical tableau into a pure and a complicated type which among other conditions encompasses mental retardation/cognitive impairments. The genetic profile is as heterogeneous as the clinical one including autosomal dominant, x-linked, and autosomal recessive mode of inheritance. HSP with thin corpus callosum(TCC) is an autosomal recessive form of the disease with a few reported cases in Japan and a limited number of Caucasian patients. According to the literature SPG11 is the most frequent of HSP with TCC, followed by SPG15 in fewer cases. Both forms share similar clinical and imaging presentations with very few distinctions.

Methods:: We present the case of a 32-year-old caucasian male, with a history of dysarthria, gait disturbance and frequent falls progressively developing into a spastic deficit of lower limbs accentuated in the second decade. The diagnostic criteria of HSP with TCC were carefully reviewed and all the clinical and radiological criteria were met. Magnetic Resonance Imaging(MRI) evidenced the thin corpus callosum with frontoparietal cortical atrophy.

Results:: To our knowledge there are very few cases of autosomal recessive HSP with TCC in Albania as elsewhere in the world.

Conclusions:: The clinical profile of HSP-TCC accompanied with a thin corpus callosum and other characteristics in MRI should be evocative to genetically investigate our patients in order to correctly address genetic counseling.
Background and Aims:: Idiopathic intracranial hypertension (IIH) is a rare neurological disorder in children. It is characterized by raised intracranial pressure in the presence of normal cerebrospinal fluid chemistry, normal neuroimaging, and no localizing signs on neurological exam (with the exception of cranial nerve VI palsy). We review clinical presentation, diagnosis and management of IIH in children.

Methods:: Retrospective review of six children with the diagnosis of IIH. All patients underwent neurological, ophthalmological and radiological exams.

Results:: Our study included six girls. The average age was 8.5 years. Three patients were in the peripubertal period. All patients complained of headache, blurred vision, often associated with vomiting. Two patients had binocular diplopia. The neurological examination was normal in all patients. Visual acuity was decreased in two patients. Bilateral papilloedema was found in all cases and two patients presented limitation in abduction. Goldmann visual field was performed in three patients and found an enlarged blind spot. Brain MRI showed partial empty sella in one patient and was normal in five patient. Lumbar puncture was done in all patients and showed a high cerebrospinal fluid opening pressure (25-51 cmH2O). The body mass index and the endocrine balance were correct. All patients received acetazolamide. The evolution was favorable in all cases.

Conclusions:: Children with suspected IIH should have careful ophthalmological and full neurological examination. IIH could be associated to hormonal changes occurring on peripubertal period. If not treated properly, IIH may lead to severe visual dysfunction.
OUTCOMES OF SELF-REGULATION IN 24-MONTH-OLD CHILDREN AFTER PEDIATRIC ARTERIAL ISCHEMIC STROKE

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Background and Aims:: The ability to self-regulation (initiation, organization and control of own activity) is one of the most important qualities of the human. Pediatric arterial ischemic stroke (PAIS) in infancy usually entails dysfunction, which can also manifest itself in difficulties of self-regulation. Objective was to assess the level of self-regulation in children with PAIS in comparison with the control group.

Methods:: Level of self-regulation was assessed using a parent questionnaire Scale "Adaptive behavior" (Bayley-III). The study involved 65 children aged 5 months and 41 children 24 months old. The control group included children without organic lesions and chronic diseases, full-term: 52 children (34 boys) 5 months (6,0±0,7 month) and 27 children (15 boys) at 24 months (25±0,8). The experimental group included children survived PAIS before 5 months of life: 13 children (8 boys) 5 months (5,9±1) and 14 children (10 boys) at the age of 24 months (25.1±1.6)

Results:: At the age of 5 months there were no significant differences between the level of self-regulation in the groups; at 24 months the differences were revealed: raw scores were 41±11 in the experimental group and 48.5±10 in the control group (t=2.4, p=0.02).

Conclusions:: Self-regulation is a systemic, integrative phenomenon, with cognitive, emotional and behavioral components (Vilenskaya 2016). Taking into account the importance of self-regulation as an integrative function, providing the child adaptation, it is important to pay attention to the recovery and rehabilitation of children with PAIS not only for the motor skills or speech development, but also for self-regulation development.
A CHILDHOOD CASE OF BAG-3 MYOFIBRILLAR MYOPATHY HEART TRANSPLANTED PRESENTING PANCREATIC TUMOR.

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Background and Aims:: A child affected by myofibrillar myopathy caused by a mutation in BAG3, a co-chaperon, presented cardiomyopathy, peripheral neuropathy, respiratory insufficiency, pancreatic tumor.

Methods:: A girl has been studied for BAG3-related cardiomyopathy by cardiac ECHO, catheterism, muscle biopsy, MRI.

Results:: This girl suffered from age 3 of exercise intolerance, was found to have restrictive cardiomyopathy by cardiac Echo, bilateral atrial dilatation, telediastolic reflow. At 11 years of age, she was diagnosed with genetic myopathy due to a mutation of the BAG3 gene, for a heterozygous variant (p.Pro290Leu.) She presented hypertrophic cardiomyopathy, peripheral neuropathy. At the neurological exam, she had a waddling gait, bilateral winging scapulae, was able to raise with Gowers' manoeuvre, showed distal weakness and wasting, erythromelalgia. Because of dyspnea, her cardiomyopathy was treated with 2.5 mg/day bisoprolol, aldactazide, she was able to sleep with one cushion, during cardiac catheterization she had systolic ventricular hypertension, elevated pulmonary pressure. Cardiac biopsy was done, that showed fibrosis, focal lymphocytic infiltrates: cardiac transplant was planned. At age 12 a muscle biopsy showed cytoplasmic bodies, rimmed vacuoles, splitting fibers, internal nuclei. At age 14 she underwent a cardiac transplant, was in ICU, and presented OSAS. Her scoliosis deteriorated. In the following months, she was immunosuppressed. Motor functions improved. A muscle MRI showed fibro-fatty substitution of the right scapular girdle, bilaterally in thigh muscles and distal leg muscles. At age 16 she presented pancreatic tumor.

Conclusions:: This BAG-3 patient was successfully heart transplanted in the follow-up she needed psychological support, subsequently a pancreatic tumor was found, possibly related to her BAG3 variant and immunosuppressive therapy.
PROGNOSIS OF SURGICAL TREATMENT OF THE TETHERED CORD SYNDROME IN CHILDREN

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Background and Aims: Purpose. The aim of this study was to identify the factors relevant to the prognosis of the outcome of the surgical treatment of the tethered cord syndrome (TCS).

Methods: Methods. The results of surgical treatment performed on 58 children with TCS were analyzed, with follow-up periods ranging from 6 months to 5 years. The data of preoperative clinical and instrumental examinations, as well as those of intraoperative electrophysiological diagnostics and morphometry, were compared with the dynamics of the TCS clinical presentation.

Results: Results. The recovery rate was significantly higher in children with filum terminale abnormality (p=0.014), as well as Grade I tethering (p=0.0037), and when the spinal cord tracts at the level of intervention were intact (p=0.018). Complete untethering (p=0.04) and a low threshold value of amperage in direct stimulation (<1 mA) (p=0.016) were identified as factors for a favourable outcome. Worsening of neurological symptoms was more frequent in children operated over the age of 10 (p=0.03), when the TCS was manifested exclusively through the pelvic dysfunction (p=0.00004), if the F-wave block is less than 30% (p=0.0045) and the stimulation threshold during root mapping ranged from 1 to 5 mA (p=0.01).

Conclusions: Conclusion. The operation is recommended when structural changes are minimal. In case of severe structural changes, if the spinal cord tracts are intact, the indications for operation are determined by the risk of irreversible structural changes due to the natural course of the disease, although the risks are substantially higher.
**BILATERAL VISUAL IMPAIRMENT AS A RARE MANIFESTATION OF ARNOLD CHIARI MALFORMATION TYPE 1**

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**Background and Aims::** This is to report a rare presesntation of bilateral diminution of vision in a case of Arnold Chiari Malformation type 1 in an young boy.

**Methods::** Four year old boy presented with bilateral progressive diminution of vision (DOV) with episodes of occipital headache with vomittings more after crying. Episodes of headache were short lasting with recurrent falls. He had history of sleep apnea also. On examination patient has scaphocephaly, bilateral optic atrophy with bilateral gaze evoked nystagmus. On neuroimaging MRI Brain revealed Arnold Chiari Malformation type 1 (ACM 1) with prominent subarachnoid space around bilateral optic nerves.

**Results::** The hypothesis for DOV was repeated episodes of raised intracranial tension during crying leading to increased pressure on both optic nerves with axonal degeneration over years. As patient was posted for posterior fossa decompression, it was postulated that further progression in optic nerve damage will be diminished.

**Conclusions::** To bring out this case is not to miss in early stage of DOV, ACM 1 as one of the etiology as early treatment can halt the progression of optic nerve axonal degeneration. Prominent subarachnoid space around optic nerves and ACM 1 are correlating radiological pearls in this particular case.
A CASE OF INFANTILE BOTULISM AND CMV COINFECTION: RED FLAGS OF AN INSIDIOUS DIAGNOSIS AND THE ROLE INTESTINAL DYSBIOSIS AND HYPOGAMMAGLOBULINEMIA AS RISK FACTORS

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Background and Aims:: Botulism is a rare pathology caused by a neurotoxin produced by bacteria of the genus Clostridium, responsible of a clinical condition characterized by flaccid paralysis and autonomic dysfunctions. Some forms, called infantile botulism, are secondary to the colonization of Clostridium botulinum spores in the gut of children and the subsequent production of the toxin. The reason why only some children develop the disease after ingesting the spores present in the environment and others not is not entirely clear, but it is probably linked to host factors. In particular, alterations of the gut microbiota, latent subclinical viral infections and alteration of immune response could be at the basis of this phenomenon, with important implications in the treatment of dysbiosis as a preventive weapon for numerous diseases, including infantile botulism.

Methods:: Herein we described the first case of infantile botulism and CMV coinfection in a 6-month-old boy.

Results:: The mechanisms by which some children develop the disease after ingesting the spores present in the environment and others not is not entirely clear, but it is probably linked to host factors. In particular, alterations of the gut microbiota, latent subclinical viral infections and alteration of immune response could be at the basis of this phenomenon, with important implications in the treatment of dysbiosis as a preventive weapon for numerous diseases, including infantile botulism.

Conclusions:: We discuss the possible role of gut microbiota alterations and immunological changes associated with CMV infection (with minor or no clinical symptoms) as risk factor for the growth of C. botulinum spores. In addition as the most probable mimicker is Guillain-Barré Syndrome (GBS), we highlight that every acute floppy infant under one year of age with clinical features of GBS with autonomic involvement, but absence of confirmatory GBS instrumental features (CSF albumin-cytological dissociation, MRI enhancement, sensory and motor involvement) should receive fast laboratory investigations also for C. botulinum in first days of admission.
ASSOCIATION BETWEEN HLA GENE POLYMORPHISM AND CUTANEOUS ADVERSE REACTIONS CAUSED BY ANTIEPILEPTIC DRUGS

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Background and Aims:: There are approximately 10 million patients with epilepsy currently in China, seriously affecting the lives of patients. Adverse drug reactions of antiepileptic drugs often occur easily, the most common of which is the cutaneous adverse drug reaction (cADR). In recent years, it has been shown that human leukocyte antigen (HLA) polymorphism has a significant correlation with the incidence of cADRs.

Methods:: Through the case-control study, 30 child patients with AED-induced cADRs (cADRs group), 60 AED-tolerant child patients (AED-tolerant group) and 60 normal children not taking AEDs (normal group) were collected. The HLA-B*15:02 and HLA-A*31:01 genotypes were detected using the polymerase chain reaction-sequence-specific oligonucleotide (PCR-SSO) probe method, and the correlation of HLA-B*15:02 and HLA-A*31:01 genes with the incidence of cADRs was analyzed.

Results:: The positive rate of HLA-A-B*15:02 gene was 83.33% in the cADRs group, which was significantly increased compared with that in the AED-tolerant and normal groups (P<0.01). The positive rate of HLA-A*31:01 gene was 63.33% in the cADRs group, which was obviously increased compared with that in the AED-tolerant and normal groups (P<0.01). There were no significant differences in HLA-B*15:02 and HLA-A*31:01 genotypes between the AED-tolerant and normal groups (P>0.05).

Conclusions:: The results showed that HLA-B*15:02 and HLA-A*31:01 are significantly associated with cADRs in a Chinese Han population in Shanghai, suggesting that HLA-B*15:02 and HLA-A*31:01 genotypes should be detected in the application of AEDs.
EFFECT OF AGE OF ONSET AND TREATMENT ON CONTROL OF EPILEPTIC SPASMS: FINDINGS FROM THE SRI LANKA INFANTILE SPASMS REGISTRY

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Background and Aims:: Objective To describe the effect of age of onset and treatment lag on response to therapy among children diagnosed with West syndrome in Sri Lanka
Methods:: Method Data was extracted from the Sri Lanka Infantile Spasm registry. Onset of spasms was considered early if onset occurred at <3 months and late if > 12 months. Treatment-lag was categorized as <14 days, 14-28 days and > 28 days. Spasm control was ascertained at 14 days and other time points.
Results:: Results There are 261 Children entered in the registry as at January 2021. Mean age of onset was 5.44 months (SD. 3.93); early in 58 (24.4%) and late in 14 (5.9%). Electroencephalography showed hypsarrhythmia in 89%, normal in 7.5%, unavailable/ not done in the balance. Most commonly known aetiologies included low birth weight (36%), neonatal seizures (31%), Birth asphyxia (15.1%). Of the three categories, largest treatment lag of >28 days reported in 44%. Majority (87%) received standard first-line therapies. Mean duration for spasm freedom was 13.2 days for first-line versus 40.5 days for non-standard therapies. First line therapies were oral prednisolone in 151(73%) and ACTH in 49(24%). Spasm control was significantly better if received prednisolone (p=0.04) Early onset of spasms (p=0.4), delayed treatment lag of >28 days (p=0.198). or male sex (p=0.37) were not associated with day 14 poor spasm control.
Conclusions:: Conclusions Data from this large cohort suggest faster control of spasms occurs with standard first-line therapies. Poor control was not associated with early onset or delayed treatment of >28 days.
SPECTRUM OF NEUROLOGICAL DISORDERS IN HIV POSITIVE PATIENTS ATTENDING A TERTIARY CARE CENTRE OF EASTERN INDIA

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Background and Aims:: Neurological complications are common in HIV and can affect any part of the neuraxis. This study was conducted to describe the different neurological disorders occurring in HIV and analyse their pattern according to the CD4 count, WHO clinical stage, duration of HIV infection, treatment status, and treatment duration.

Methods:: 61 HIV-positive patients who had neurological involvement were included. Demographic parameters, clinical findings, investigations, duration of HIV, CD4 count, WHO stage, ART regimen, and its duration were recorded. Written consent was obtained.

Results:: 39 patients were male and the median age was 36 years. 36 patients were taking ART, TLE being the most common regimen (80.55%). Neurological disorder was the presenting manifestation of HIV in 23% of patients. The most common diagnosis was CNS tuberculosis (27.8%), followed by distal symmetric polyneuropathy (13%), and progressive multifocal leukoencephalopathy (11.5%). The median CD4 count was 172 cells/mm³. 59% of the disorders occurred below CD4 count of 200 cells/mm³. 64% of patients were in WHO stage 4. The median duration of HIV was 3 months and 52.5% of cases occurred within 3 months. 37.5% of disorders were direct HIV-related, while 54.7% were due to opportunistic infections. Opportunistic infections occurred significantly more compared to direct complications in WHO stage 4 (p<0.0001), CD4 count <200 cells/mm³ (p=0.004), within 6 months of HIV diagnosis (p=0.002), in patients not on ART (p= 0.004), and within 6 months of ART initiation (p=0.03).

Conclusions:: Various neurological disorders can occur in HIV. Despite widespread ART use, opportunistic infections are still prevalent.
Background and Aims:: Neurosyphilis can present with wide variability of central nervous system manifestations making difficult reaching a correct diagnosis. In addition, features of neurosyphilis that mimic herpetic or autoimmune encephalitis have been described. We present two patients whose clinical manifestations were suggestive of encephalitis.

Methods:: Patient 1. A 54-year-old man presented with a language disturbance, mainly consisting in speech arrest, started 6 months prior and later associated to ideomotor slowing, cognitive impairment and ataxic gait. A brain MRI was normal. EEG arose the hypothesis of non-convulsive status epilepticus and treatment with levetiracetam was started. The patient’s seizures disappeared, while the cognitive difficulties persisted. Patient 2. A 45-year-old man was brought to the emergency room because of a generalized tonic-clonic epileptic seizure. For some days he had been complaining of headache and dizziness. His EEG showed an electrographic seizure and interictal epileptiform discharges in the right hemisphere. Brain MRI revealed high signal in bilateral mesial temporal lobes.

Results:: Cerebrospinal fluid (CSF) analysis demonstrated in both patients elevated proteins and pleocytosis leading to consider an infectious or autoimmune/paraneoplastic etiology for their subacute encephalopathy. However, the screening for all these conditions was found to be negative, while serologic and CSF tests for syphilis were positive. Both patients were successfully treated with a 14-day course of Cetriaxone.

Conclusions:: The presented cases outline that neurosyphilis may mimic herpetic and autoimmune encephalitis. This possibility should be considered because its early recognition and treatment are crucial to prevent further progression of the disease and allow the recovery.
A RARE CASE OF LISTERIA RHOMBENCEPHALITIS WITH A SUDDEN CLINICAL ONSET AND UNUSUAL MRI FEATURES

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Background and Aims:: Listeria rhombencephalitis is a very rare and fatal CNS infections. Here we describe a peculiar case of listeria rhombencephalitis with a sudden clinical onset and uncharacteristic radiological findings.

Methods:: Case Report

Results:: A 66 years-old female presented with a sudden onset of unsteadiness, dysarthria, left arm weakness, acute fever up to 39 °C and recurrent vomiting. Her medical history was significant for pancreas carcinoma (stage III) on neoadjuvant chemotherapy. Laboratory tests revealed leucocytes 33.50 x10.9/L, neutrophils 31,5 x10.9/L, deranged LFTs, CRP 16.60 mg/L and negative procalcitonin. Brain-CT scan was unremarkable. GCS was 15. Within few hours of admission, a rapid neurological deterioration was observed, with fluctuating consciousness and muticism, dropping to a GCS of 11. Neurological examination revealed inconstant execution of simple motor task, deviation of head and eyes to the left side, pinpoint pupils slightly reactive to light, absent corneal reflex, left side paresis, along with mild meningeus. Soon after, she developed an acute respiratory distress, so orotracheal intubation was performed. CSF examination revealed a leukocyte count of 372/mm³ (90% neutrophils), a protein concentration of 247 mg/dl and a glucose concentration of 4.2 mmol/L. CSF-PCR was positive for L. monocytogenes, while CSF culture was unrevealing. A 3T Brain-MRI showed gross brainstem involvement with associated hemorrhage, suggestive of rhombencephalitis.

Conclusions:: Our case is worth of consideration for the MRI findings, showings an extensive hindbrain involvement, instead of more typical abscesses with ring enhancement. Moreover, the sudden onset, not preceded by a prodromal phase is an atypical presentation preluding a devasting clinical course.
Background and Aims:: Introduction Neurocysticercosis(NCC) is a rare neurological disorder caused by the larval stage of the pork tapeworm Taenia solium (TS). Even though cysticercosis is endemic in India it has not been reported from Sri Lanka in an adult

Methods:: Case Report A 29 year old man presented with chronic headache and adult onset epilepsy. He was well before headache set in 18 months ago. Neurological examination including fundi was normal.

Results:: His haematological and biochemical evaluation was normal. His CSF too was normal .MRI brain revealed multiple focal lesions in bilateral cerebral hemispheres. On T2 MRI images these lesions had a target appearance due to multiple alternating signal intensities. All lesions enhanced with gadolinium. The MRI appearance was characteristic of parasitic infection due to NCC with lesions of different stages. TS antibodies were negative in both serum and CSF. Repeat MRI brain imaging showed new lesions appearing whilst some old lesions disappearing. With the clinical history and neuroimaging findings suggesting NCC, the patient was started on Albendazole 15mg/kg daily dose with steroids, dexamethasone 0.1 mg/kg/day. The treatment was continued for 14 days. Within 2-3 days of initiation of treatment, there was significant improvement in headache. Post treatment MRI showed near complete resolution of the previous lesions without any new lesions.

Conclusions:: Even though serological diagnosis of cysticercosis may be difficult, a proper clinical evaluation together with imaging findings will lead to the diagnosis of NCC. It is interesting as to why an infectious disease endemic in neighbouring India is so uncommon in Sri Lanka.
Background and Aims:: Central nervous system (CNS) infection is associated with high rates of morbidity and mortality, and despite advancements in molecular testing, aseptic meningitis remains challenging to diagnose. Aseptic meningitis cases are often underreported worldwide, which impacts the quality of patient care. Therefore, we aimed to assess the results of BioFire® FilmArray® meningitis/encephalitis (ME) PCR panel, clinical characteristics, and etiologies of aseptic meningitis patients.

Methods:: From January 2018 to January 2020, all pediatric and adult patients in a large tertiary medical center who underwent lumbar puncture and cerebrospinal fluid (CSF) testing by a ME multiplex PCR panel and who fit the aseptic meningitis definition were retrospectively reviewed.

Results:: Data were reviewed from 1,607 patients; 240 met the inclusion criteria (54.6% males; 68.8% <4 years of age). The rate of detected viral causes of aseptic meningitis was 40.4%; therefore, 59.6% of the patients remained with unidentified etiology. Among the identified viral meningitis, enterovirus and human herpesvirus 6 (HHV-6) were the most common (25 and 7.9%, respectively). The median length of hospital stay was 6 days, and it was longer in patients with unidentifiable aseptic meningitis (p < 0.0001).

Conclusions:: Aseptic meningitis is common among suspected meningitis patients, but most cases remained of unknown etiology. The most common identified viruses were enterovirus followed by HHV-6, and there is predominance in males and the pediatric age group. These results highlight that further research is needed to identify other etiologies and possible additional viral pathogens for aseptic meningitis in the current diagnostic methods.
LONG SEGMENT MYELITIS SECONDARY TO NEURO MELIOIDOSIS

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Background and Aims:: Neuro melioidosis, comprising approximately 4% of all cases of melioidosis carries a high mortality and morbidity. Long segment myelitis due to melioidosis is very rarely reported. We describe a Sri Lankan male who presented with long segment myelitis secondary to melioidosis.

Methods:: 47 year old previously healthy male presented with progressively worsening quadriplegia with bladder and bowel involvement. He also had intractable hiccups. Neuro exam revealed flaccid quadriparesis.

Results:: Initial hematological investigations and inflammatory markers were normal. CSF protein was elevated (76mg/dl) with a significant sugar drop (72mg/dl (RBS 159 mg/dl)) without a cellular reaction. CSF TB gene X pert testing was negative. Initial MRI spine revealed long segment myelitis with post contrast enhancement extending from lower medulla up to D10 level. Rest of the MRI brain was normal. The patient was started on IV MPP followed by TPEs without significant improvement. His repeat MRI revealed abnormal high signal in brain stem and whole spinal cord with contrast enhancement. A repeat CSF study revealed protein 1187 mg/dl, sugar 78 mg/dl (RBS 198) with lymphocytes 1600/mm3 and neutrophils 10200/ mm3. CSF culture become positive for Burkholderia pseudomallei. Serum melioidosis antibody titre was 1:160. The patient was started on IV meropenem with oral cotrimoxazole.

Conclusions:: Even though various neurological manifestations have been described due to melioidosis, long segment myelitis with positive CSF culture has not been described. This case highlights the importance of considering melioidosis as a differential diagnosis in patients with long segment myelitis in the endemic areas in addition to other known causes.
MENINGOVASCULAR SYPHILIS IN RECURRENT STROKE: A CASE REPORT

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Background and Aims:: Syphilis is a known cause of tardive vasculitis which has preference over aortic and intracranial vessels. It may lead to vascular deficit and subsequent stroke.

Methods:: We present a case report whose diagnosis, treatment and ultimate follow-up was carried out by our Neurology and Infectious Diseases Departments.

Results:: A 38-year old man with known HIV infection presented to the Emergency Room with mild right hemiparesis. Complementary tests showed acute left pontine stroke along with parietal thickening and narrowing of the basilar artery, suggestive of inflammatory process. Serum VRDL and cerebrospinal fluid VRDL both tested positive. The patient received intravenous penicillin G for 21 days and was discharged with residual paresis. Five months later the patient returned with a new left pontine stroke and critical stenosis of the middle segment of the basilar artery, and was discharged under dual-antiplatelet therapy, given the fact that endovascular approach was unfeasible. This could not prevent the patient from having a new right medullary stroke one month later, which left the patient with severe left hemiparesis.

Conclusions:: Considering the recent rise in the incidence of syphilis in the West, the diagnosis must be considered in strokes of initially undetermined causes. Meningovascular syphilis and the subsequent obliterative endarteritis is the most common clinical variety of neurosyphilis. The present case illustrates the clinical presentation of meningovascular syphilis and depicts how difficult to control and treat the disease can be even using standard antibiotherapy.
SKULL BASE OSTEOMYELITIS: CLINICAL PREDICTORS AND OUTCOMES

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Background and Aims:: Background: Skull base osteomyelitis (SBO) is an enigmatic clinical diagnosis which is difficult to decipher and is associated with poor outcomes. Aim: The study aims to examine the demographic and clinical characteristics of patients with SBO and its outcomes.

Methods:: Material and Methods: Medical records of thirty patients with diagnosis of SBO over last five years were assessed for demographic and clinical characteristics, type of SBO, radiological parameters, treatment received, diagnostic or therapeutic procedure performed, microbiological profile, comorbidities and complications including cranial nerve palsies. These factors were analysed for prediction of outcome (death or survival).

Results:: We found SBO was the disease of elderly population (64.07±6.13 years) with male predominance (83.3%) highly associated with uncontrolled diabetes status (93.3%). Headache (100%) and cranial nerve palsy (80%) were the most common neurological presenting complaints followed by stroke (17%) and encephalopathy (10%). Pathological and radiological correlation showed that fungal infection (aspergillus) was associated with anterior SBO (10%) while bacteria (pseudomonas) was cultured from posterior SBO (30%). Fifty percent patients were alive after one year out of which 33% had good functional outcome. The mortality rate was 33.3% in our cohort and multiple lower cranial nerve palsies (P=0.04), sub-optimal duration of medical treatment (P=0.03), surgical intervention during clinical course (P=0.02) and development of intracranial or extracranial complications (P=0.03) were the predictors of mortality.

Conclusions:: Discussion: Early recognition of this condition including identification of pathogenic organisms and optimal duration of treatment are crucial for improved
outcomes.
Background and Aims:: Introduction: Parotid gland involvement as a form of extra pulmonary tuberculosis is a very rare manifestation. Extension of tuberculosis to skull base with multiple cranial nerve involvement is even rarer. We report a case of atypical presentation of tuberculosis with multiple cranial nerve palsies.

Methods:: Case: A previously healthy 40-year-old woman presented with progressive dysphagia and deviation of mouth to left for one-week without a history of fever, chronic cough, or headache. On examination she had bilateral nontender asymmetrical parotid enlargement without cervical lymphadenopathy. Nervous system examination revealed right sided lower motor type of facial nerve palsy, right palatal palsy and weakness of left sternocleidomastoid and trapezius with wasting.

Results:: ESR was 40mm/1st hour. Cerebrospinal fluid analysis showed elevated protein of 143mg/dl with lymphocyte count of 10/cu mm. Sputum for AFB, Mantoux test and tuberculosis PCR were negative. Serum ACE level was normal. MRI brain showed enhancing thickened right cranial nerve (CN) VII and left CN XII. Excision biopsy of left parotid gland showed caseating granulomatous inflammation. Retroviral antibodies were negative. She was empirically started on anti-tuberculosis treatment for one year without corticosteroid. During the first three months of treatment, parotid swelling had regressed, and dysphagia and facial nerve palsy had improved remarkably.
Conclusions:: Even though the caseating granulomatous inflammation is characteristic of tuberculosis, sarcoidosis also can rarely give rise to it. Our patient responded well to anti tuberculosis treatment without corticosteroids clearly supported the diagnosis of tuberculosis. Diagnosis of tuberculosis with atypical presentation needs a high degree of clinical suspicion.
BRAIN VOLUMETRIC CHANGES AND ITS ASSOCIATION WITH COGNITIVE OUTCOME IN TUBERCULOSIS MENINGITIS PATIENTS – A LONGITUDINAL STUDY

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Background and Aims:: Studies on brain volumetric analysis and neuropsychiatric impairment in patients with Tubercular Meningitis (TBM) are limited and none with long term follow up.

Methods:: This prospective study was conducted between 2017 to 2019. Total of 29 adults with TBM (definite-8, probable-21) were included. Volumetric changes on Brain MRI and cognitive profile by eight neuropsychological tests were analyzed and compared at baseline and at 1 year.

Results:: Mean Total Intracranial Volume(TIV), Grey Matter(GM) and White Matter(WM) volume at baseline were 1298.43 ±126.68cm³, 598.67± 58.11 cm³, 414.00 ± 48.13 cm³ respectively. Mean cortical thickness was 2.70±0.09mm. At 1 year of follow up, mean TIV, GM and WM volume were1321.97±126.06 cm³, 615.34±55.36 cm³, 413.62± 43.04 cm³, 2.76± 0.08mm. There was no significant difference between gray matter, white matter volume, however cortical thickness was more at the end of 1 year of follow up, mainly in definite TBM (p=0.005). On comparing GM volumes of different areas at baseline and follow up, by Montreal Neurological Institute (MNI) coordinates, significant volume differences were noticed in temporal and frontal areas mainly hippocampus, superior frontal gyrus, and occipital gyrus, all on the left side. Neuropsychological tests done at baseline were suggestive of frontal and temporal region involvement, predominantly involving areas as observed with MNI coordinates with better recovery of frontal lobe functions during follow up.

Conclusions:: On morphometric analysis, cortical thickness was high suggesting persistence of inflammation with grey matter involvement and eventual development of cognitive disturbances. This was confirmed by neuropsychological tests as evidence by impaired left fronto-temporal lobar functions.
PARTIAL OCULOMOTOR NERVE PALSY AS THE SOLE SYMPTOM OF NEUROBORRELIOSIS

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Background and Aims:: neuroborreliosis is a tick-transmitted multisystem inflammatory disease. Neurological complications have been reported, including meningitis, facial nerve palsy, and peripheral neuropathy. Isolated oculomotor nerve palsy is rarely seen.

Methods:: We report a case of neuroborreliosis manifesting with isolated oculomotor nerve palsy and we describe outcome after instauration of antibiotic therapy.

Results:: A 58 year old man, without past medical history, was presenting at our department of neurology with a newly acquired partial ptosis and deviation of the left eye. The past 2 weeks he had suffered from intermittent headache. No tick bite exposure has been reported. Neurologic examination revealed a palsy of the third cranial nerve. There was no pupillary dysfunction and no further cranial nerve palsy was observed. The rest of his physical and neurological examinations were normal. Magnetic resonance imaging (MRI) with angiography (MRA) did not show any abnormalities. Routine blood examination was normal. Cerebrospinal fluid (CSF) analysis did not reveal pleocytosis with normal proteins. The oligoclonal bands were not detected in the CSF. Auto immune antibodies and infectious tests were negative. Serum anti-Borrelia burgdorferi IgG- and IgM were positive. The diagnosis of Lyme Borreliosis was established. The patient was treated with oral doxycycline 200 mg per day for 21 days. Two months after antibiotic and orthoptic treatment, the ocular movement improved and ptosis definitively disappeared.

Conclusions:: This case is an example of unusual presentation of neuroborreliosis. Clinicians should consider Lyme disease for any idiopathic oculomotor nerve palsy.
PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY IN AN EVER-TREATED PULMONARY SARCOIDOSIS

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Background and Aims:: PML has been described in various immunological diseases, usually in patients receiving immunosuppressive therapies. We describe a case of PML in an ever-treated pulmonary sarcoidosis.

Methods:: A 60-year-old Italian male patient, affected by pulmonary sarcoidosis under no treatment, was referred to us because, one month earlier, started noticing loss of memory, aphasia nominum and cognitive slowing. Neurological examination revealed cognitive-motor slowing, mild right hemiparesis, right-sided hyperreflexia and mild coordination ataxia. Routine laboratory exams were unremarkable; TPHA and HIV tests were negative. CSF cell count, protein and glucose levels were normal. PCR testing for CMV, EBV, HSV 1-2, VZV replication was negative; no oligo-clonal bands nor paraneoplastic antibodies were detected.

Cranial
MRI revealed large hyperintense areas on T2-weighted images in the subcortical white matter of both frontal lobes, with no contrast enhancement. Thinking of an atypical neurosarcoidosis, corticosteroids were initiated. During the hospitalization clinical conditions worsened, a CSF exam was repeated and JCV-specific DNA detected, without JCV replication in blood. Corticosteroids were immediately suspended and empirical therapy with Mirtazapine was initiated. Unfortunately, the progression was very rapid, with the early development of right spastic hemiparesis, sphincter incompetence and severe dysphagia quickly
leading the patient to death.

**Results:** The clinical, virological and imaging findings were consistent with PML, even though at first misdiagnosed due to the concurrent sarcoidosis and the absence of immunosuppressive therapy.

**Conclusions:** Even if it's rare, PML should always be investigated because its physiopathological pattern is not well-established, not knowing if the cause is primarily the immunosuppressive therapy or the disease itself.
Background and Aims:: SSPE is a chronic progressive encephalitis due to persistent measles viral infection. Clinical features, neuroimaging, EEG, CSF and serum measles antibody levels assist in the diagnosis. We report a case of SSPE confirmed by CSF measles antibodies and MRI abnormalities but without myoclonus or characteristic EEG changes.

Methods:: 35-year-old female presented with acute blindness worsening over two weeks. Rest of the neurological exam was normal with no evidence of optic neuritis or papillitis. Brain MRIs (Figure 1) showed progressive involvement of white matter extending from occipital region to frontal cortex. Patient gradually lost cognitive and motor skills. Measles antibodies were suggestive of SSPE (Table 1), Serial EEGs persistently showed only non-specific mild patchy background slowing which remained same. Brain biopsy was consistent with panencephalitis. A diagnosis of SSPE was made. No known classical EEG changes appeared over a one year follow up period. Vaccination history was uncertain. She was treated with alpha Interferon, Ribavirin and intrathecal
Isoprinosine.

Figure 1: A, B, C, D, E, F: T1 flare images showing rapid occipital to frontal progression of hyperintensity.
Results: The diagnosis of SSPE is mainly based on Dyken’s criteria (Table 2). EEG can be normal or generally slow in the early stages of SSPE but with time EEG evolves showing the characteristic ‘myoclonic’ pattern and later increasingly disorganized with high amplitudes and random dysrhythmic slowing.

<table>
<thead>
<tr>
<th>CSF Oligoclonal bands</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF antibody titer</td>
<td>&gt; 1/4</td>
</tr>
<tr>
<td>Serum antibody titer</td>
<td>&gt; 1/256</td>
</tr>
<tr>
<td>CSF to serum antibody ratio</td>
<td>1/25 (more than 1/100)</td>
</tr>
</tbody>
</table>

Table 1

Conclusions: To best of our knowledge, there are no reported cases of SSPE with normal or near normal EEGs occurring throughout the course of the illness over one year. This finding made the diagnosis difficult in this case.

Table 2: Dyken’s criteria
Definitive: criteria 5 and three more criteria
Probable: three of the five criteria
1) Clinical – Progressive, subacute mental deterioration with typical signs like myoclonus
2) EEG - periodic, generalized, bilaterally synchronous and symmetrical high-amplitude (300–1500 μV) slow waves 0.5- to 2-seconds that recur at regular intervals of 5–15 s called Radermecker complexes
3) Cerebrospinal fluid – Raised globulin (greater than 20% of the total CSF protein) or oligoclonal bands
4) Measles antibodies – Raised titer in serum (>1/256) and/or CSF (>1/4)
5) Brain biopsy – Suggestive of panencephalitis
Background and Aims:: Tuberculosis (TB) is a common infection worldwide. Approximately one third of the entire world population is infected with TB. Involvement of spinal cord and spinal nerve root is one of the leading causes of disability in these patients and it has a significant impact on morbidity and mortality. Through this study we aim to study the incidence, prognosis and impact of different types of spinal cord involvement in patients of CNS TB.

Methods:: Prospective observational study.

Results:: Current study included 99 patients of TBM. The commonest clinical features were fever(100%), headache(94.9%) and vomiting(70.7%), loss of weight/appetite(71.7%) and seizures(26.3%). Clinically, meningeal signs(94.9%), altered sensorium(62.6%), and focal deficits were most common. Clinical evidence of spinal cord involvement was found in 22 patients. MRI spine was abnormal in 61.6% of patients, including arachnoiditis(47.5%), isolated root enhancement(8.1%) and Pott's spine(6.1%) patients. All the patients were treated with standard antitubercular therapy as per guidelines. Presence of hydrocephalus, infarcts, exudates, and tuberculomas, and spine involvement correlated highly significantly with final outcomes. Positive influence of clinical and radiological evidence of cord/ root involvement on poor outcome as defined by mRS(p=0.01)

Conclusions:: Spinal disease in form or cord/ root or bone involvement is common in patients with CNS TB being seen in approximately 61.6% of all patients. Most common abnormality is in form of arachnoiditis. Clinical and radiological evidence of spinal disease is associated with poor functional recovery in CNS TB.
COMPARISON OF DEXAMETHASONE REGIMENS IN TUBERCULAR MENINGITIS (TBM): A RANDOMIZED OPEN LABEL CLINICAL TRIAL

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Background and Aims:: Corticosteroids are used as adjunctive treatment in tuberculous meningitis (TBM). There is no universally accepted regimen of steroid administration. It is also not known about the optimum duration and route of steroid administration. Overlapping intravenous with oral dexamethasone versus directly switching intravenous to oral dexamethasone has not been compared in TBM. We aimed to study two regimens of dexamethasone: overlap oral steroid (OOS) arm and a direct oral steroid (DOS) arm, via a randomized controlled trial.

Methods:: In a randomized open labelled study, patients with TBM were divided into overlap oral steroid (OOS) arm and a direct oral steroid (DOS) arm. The primary outcome was the proportion of patients with symptomatic resolution at one month. The secondary outcomes were mortality and modified Rankin Scale (mRS) at three and six months.

Results:: Fifty-three (53) TBM patients were randomized. The symptomatic resolution at one-month in OOS (71.4% (15/21)) versus DOS ((85.0% (17/20) arm) was similar (p value: 0.45). Median mRS was 2.5 (IQR:1.0;6.0) in the OOS arm versus 1.0 (IQR: (0.0;4.0) in the DOS arm (p value: 0.31) at six months. The mortality at six months was 31.8% (7/22) in the OOS arm versus 20.0% (4/20) in the DOS arm (p value: 0.49).

Conclusions:: The outcomes were similar with both regimens in terms of achieving symptomatic resolution at one, three and six months in patients of TBM. Furthermore, there was no difference in morbidity and mortality at three and six months. These results are applicable to stage I, II and III TBM.
PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY AFTER DARATUMUMAB IN MULTIPLE MYELOMA: A CASE REPORT.

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Background and Aims:: Progressive multifocal leukoencephalopathy (PML) is a rare severe central nervous system (CNS) opportunistic infection usually occurring in immunocompromised patients. Iatrogenic PML has been described in patients assuming treatment suppressing immune surveillance in CNS. Daratumumab is an anti-CD38 monoclonal antibody, used to treat Multiple Myeloma (MM), causing the destruction of suppressive cells and the increase of CD4+ helper and CD8+ cytotoxic T cells. Only two cases of PML on daratumumab has been reported in literature.

Methods:: We report a case of PML in a patient affected by MM who started daratumumab treatment two months before our observation.

Results:: The patient was a 69 years old woman who experienced subacute onset of left hemiparesis and dysarthria followed by status epilepticus. A diagnosis of right frontal ischemic lesion was suggested on the emergency CT scan. The clinical course was rapidly progressing. Daratumumab was suspended. Cerebrospinal fluid (CSF) PCR demonstrated JCV DNA in the CSF. Brain MRI showed a large edematous frontal T2-hyperintense, T1-hypointense lesion with peripheral and patchy Gd-enhancement. PML-immune reconstitution inflammatory syndrome (IRIS) was diagnosed. Intravenous methylprednisolone was started, but the patients died within one month.

Conclusions:: PML is a life threatening condition often complicated by PML-IRIS in patients ongoing immunosuppressive treatment. PML cases under Daratumumab has been rarely reported. Since no specific PML treatment are available the unique treatment approach for such a condition is the restoration of the host's adaptive immune response. A close proactive surveillance aimed to an early diagnosis allowing early treatment discontinuation is challenging for hematologists and neurologists.
**Background and Aims::** Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis, which adds considerably to global morbidity and mortality. Intracranial tuberculoma remains a significant cause of intracranial mass lesion. It can occur anywhere in the brain with diverse clinical symptoms. Disseminated tuberculosis resulting from the lymphohematogenous spread of Mycobacterium tuberculosis in two or more contiguous sites is a debilitating disease. Although frequently reported in immunocompromised patients, we encountered a case of disseminated tuberculosis with pulmonary and renal involvement and multiple intracranial tuberculoma in an immunocompetent patient.

**Methods::** Case Report

**Results::** A 48-year-old gentleman, hypertensive for five years, presented with acute onset gait unsteadiness which was slowly progressive for the past 10 days. He was getting tired of doing his everyday routine tasks, and he had the tendency to sway to the side while walking. CNS examination revealed bilateral cerebellar signs with brisk deep tendon reflexes. MRI brain with contrast showed multiple ring-enhancing lesions of varying size in the bilateral cerebellar, cerebral hemisphere, and in the brainstem with perilesional edema. CT chest showed non-homogeneous density in the left upper lobe with small cavities and reticulonodular densities in bilateral lung fields with adjacent pleural thickening. Based on the clinical history, examination, and imaging findings, anti-tuberculous drugs and steroids were initiated. His MRI was repeated after 3 months which showed resolution of lesions along with clinical improvement.

**Conclusions::** Our case report highlights the extensive involvement of CNS tuberculosis in an immunocompetent individual and prompt resolution of clinical symptoms and recovery with appropriate treatment.
ACUTE LYME NEUROBORRELIOSIS FOLLOWING COVID-19 VACCINATION: JUST AN UNLUCKY TEMPORAL CORRELATION?

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Background and Aims:: Diagnosis of Neuroborreliosis is often challenging and requires an extensive investigation, especially in atypical cases. Herein we report a case of rhombencephalitis developed eight days after Vaxzeria vaccine. Criteria of possible acute Neuroborreliosis were fulfill and other causes ruled out.

Methods:: A 38 years-old healthy woman was admitted to emergency room for fever, drowsiness and mental confusion. The day after her symptoms worsened and neurological examination revealed mild deficit of right VII cranial nerve, ataxia, dysphagia and slurred speech. A diagnosis of rhombencephalitis was made. Lumbar puncture showed lymphocytes pleocytosis (119 white cells/mm³) and mild increase of proteins (53 mg/dL, range 15-45), while cerebral MRI was negative. Impairment of bilateral R2 response at blink reflex confirmed a brain steam involvement. A broad microbiological and immunological search performed on serum and CSF was unremarkable, except IgM for Borrelia (both enzyme immunoassay and immunoblot) and Coxiella Burnetii. Borrelia specific intrathecal antibody and polymerase chain reaction on CSF resulted negative, CXCL13 was not performed. Acyclovir and ampicillin treatment were started and when microbiological result was available we switched treatment to parenteral ceftriaxone.

Results:: Symptoms drastically improved in the following three weeks and patient was thereafter discharged with only mild cerebellar signs.

Conclusions:: Clinical course and response to antibiotic treatment support diagnosis of acute Lyme Neuroborreliosis, in addition IgM positivity for Coxiella Burnetii is a further clue for previous exposure to tick borne. The covid-19 vaccination doesn’t seem to have a casual correlation, but immune system engagement may have had a role.
PRIMARY WHIPPLE DISEASE OF THE BRAIN: CASE REPORT WITH LONG-TERM CLINICAL FOLLOW-UP

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Background and Aims:: Whipple disease (WD) is a rare multisystem disorder caused by infection with Tropheryma whippelii. Central nervous system involvement is a quite common feature observed in 20–40% of cases, whereas only 4% of patients has an exclusively neurological presentation.

Methods:: We linked the information about our patient with a literature review of patients with WD with neurological manifestations to elucidate the clinical features and diagnosis of neuro-whipple disease.

Results:: We report the case of a 53-year-old man with no medical history who consulted with a 2-month history of eye movement disorder, progressive mild cognitive decline and sleep disturbances. The patient also reported a loss of appetite and gradual weight loss. The examination showed oculo-masticatory myoryhythmias, bilateral vertical gaze palsy, skin hyperpigmentation and brittle nails. Brain MRI was normal. He also underwent a total-body CT scan which detected retroperitoneal and mesenteric lymphadenopathy and right sacroiliac ankylosis. Laboratory serological tests showed a biological inflammatory syndrome. Blood smear and routine CSF analysis were normal. Neuro-Whipple disease was then suspected and it was confirmed by the duodenum biopsy. Our patient was treated with IV ceftriaxone for 4 weeks, followed by oral doxycycline and hydroxychloroquine with a marked improvement.

Conclusions:: This case emphasizes the need to consider WD within the differential diagnosis of patients with movement disorders, cognitive impairment or sleep disturbance of unclear origin or with normal brain MRI because it is a potentially treatable disease.
CHARACTERISING A COHORT OF ENCEPHALITIS PATIENTS: AN EXPERIENCE FROM A SOUTH EAST LONDON TRUST

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Background and Aims:: Encephalitis is inflammation of the brain parenchyma; the aetiology is commonly infectious, autoimmune or unknown. The estimated incidence rate in England is 2-8 cases/100,000/year. Patients present with symptoms of reduced consciousness, seizures, psychiatric symptoms or cognitive impairment. To aid the diagnostic process neuroimaging, lumbar puncture, EEG and antibodies targeting surface or intranuclear antigens are commonly used. Prompt treatment within 48 hours reduces the mortality and chronic physical and neuropsychological sequelae. The aim of the study was to explore clinical characteristics in a cohort of encephalitis patients. Our cohort included patients admitted in a district general hospital at south east London.

Methods:: A retrospective cohort study of patients who were diagnosed with encephalitis across two district general hospitals in South East London were enrolled in the study. 94 patients which met the encephalitis criteria were included in the study.

Results:: More than 90% received intravenous acyclovir. Cases of autoimmune encephalitis (n=8) were treated with either intravenous immunoglobulins or plasmapheresis. The average number of days of admission was 26 days. 27 patients were admitted to the intensive care unit and 11 patients died. On discharge the majority of cases had some disability (modified rankin scale 2). 40% received at least 1 follow up appointment.

Conclusions:: The adherence to encephalitis guidelines need to be improved to aid prompt diagnosis and appropriate management of the patient. These patients have significant morbidity and require close follow up after the admission.
DIAGNOSTIC GRID FOR PREDICTION OF INFARCTION IN PATIENTS WITH TUBERCULOUS MENINGITIS

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Background and Aims:: TBM is commonest CNS-infection and poses significant diagnostic-management challenges in the developing countries-India.

Methods:: A total of 300 patients diagnosed with TBM were screened and out of which n=129 were recruited in the study and n= 171 patients were excluded (n=55 refused for CSF examination, n=65 had disseminated TBM and n=51 did not match inclusion criteria). Inclusion Criteria: Early TBM: Diagnosed within a month of onset IA). Not on ATT. IB). On ATT for one week Late TBM: Diagnosed after a month of onset IIA). Not diagnosed till presentation IIB). Diagnosed-not started on ATT

Results:: Table 1. Clinical scores Group I & II TBM-patients.

<table>
<thead>
<tr>
<th>Group</th>
<th>On admission</th>
<th>3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GCS</td>
<td>BI</td>
</tr>
<tr>
<td>IA (n=27)</td>
<td>11.7+ 6.5</td>
<td>69.4+ 5.6</td>
</tr>
<tr>
<td>I B (n=13)</td>
<td>12.1+ 2.6</td>
<td>67.1+ 7.8</td>
</tr>
<tr>
<td>IIA (n=26)</td>
<td>11.3+ 7.5</td>
<td>69.1+ 13.2</td>
</tr>
<tr>
<td>IIB (n=39)</td>
<td>9.5+1.3</td>
<td>50.5+ 12.3</td>
</tr>
</tbody>
</table>

Table 2. Biomarkers of all TBM patients who developed STROKE

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Pre stroke (mean)</th>
<th>Post stroke (mean)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF-a</td>
<td>311.2 + 63.6</td>
<td>606.6 + 112.3</td>
<td>0.0002</td>
</tr>
<tr>
<td>IFN-g</td>
<td>20.1 + 6.2</td>
<td>35.5 + 8.2</td>
<td>0.003</td>
</tr>
<tr>
<td>TGF-b</td>
<td>17.6+ 2.6</td>
<td>33.5 + 8.2</td>
<td>0.006</td>
</tr>
<tr>
<td>IL 6</td>
<td>30.5+ 6.7</td>
<td>44.7 + 13.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>IL 8</td>
<td>21.2+ 7.02</td>
<td>37.1 + 9.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>IL 10</td>
<td>28.8 + 8.3</td>
<td>41.6 +11.9</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusions:: Patients with TBM having low Glasgow coma scale score on presentation and presence of exudates have a significantly high risk for development of infarction.
Background and Aims:: TBM has the highest morbidity and mortality, chiefly in the initial few days to weeks and therefore it is important to modify the principles of the treatment to prevent this. AIMS To observe if administration of Linezolid along with four drug standard weight ATT based regimen in intensive phase of treatment in TBM will be safe and help reduce mortality and morbidity at 1 and 3 months among patients with TBM when compared to standard ATT alone.

Methods:: Patients with TBM were screened and recruited after obtaining a written and informed consent, if they fulfilled the criteria. Patients were randomized in a 1:1 ratio into two treatment groups either to receive standard ATT alone (control group); or add on 600 mg BD linezolid daily for 4 weeks along with conventional four drug weight based ATT[ HRZE/S]. A total of 26 patients were randomized, (14 in intervention and 12 in the control arm).

Results:: There was no difference in the two groups in the baseline characteristics . There was no significant difference between two groups in terms of mortality at one and three months and morbidity at three months . However there was significant shift towards a favourable mRS at one month and a statistically significant improvement in mean GCS score at day 14 and 30 post randomization in the linezolid arm.

Conclusions:: There was no difference between mortality and morbidity between linezolid and control arms at one and three months . Study with a larger sample size is required.
MENINGITIS AND INFECTION DISSEMINATED BY MYCOBACTERIUM BOVIS ASSOCIATED WITH CONSUMPTION OF NON-PASTEURIZED DAIRY, AN INCREASINGLY FREQUENT DISEASE IN MEXICO.

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Background and Aims:: Tuberculosis is a public health problem, with high morbidity and mortality; M. bovis causes tuberculosis in humans, livestock, and primates. Primary infection can occur through ingestion of unpasteurized dairy products and inhalation of aerosols.

Methods:: We studied the characteristics of neuroinfection and dissemination of mycobacterium bovis in 12 patients.

Results:: Twelve patients were studied, with a mean age of 30 years. Among the risk factors it was found that they had consumption of unpasteurized dairy products in 7, HIV in 6, diabetes 3, lupus 1, pregnancy 1. In ten patients the chest X-ray was observed without alterations; however, when performing a washing liquid study bronchial, a positive Lowestein culture was found. The neurological manifestations presented were headache, seizures, hallucinations, cognitive, sensory and motor deficits. Six patients required management in intensive therapy. The isolation of M. bovis was performed in CSF in 10/11; lung 9/10, urine 8/11; and in ascites, bone marrow, skin, ganglion and brain abscess. In all cases, M bovis showed intrinsic resistance to pyrazinamide, in four patients resistance to two or more drugs was demonstrated, for which a second-line drug treatment was administered. Eight patients showed resolution of the disease.

Conclusions:: Tuberculosis by M bovis in people with immunocompromised there is a greater risk of dissemination of the disease, an exhaustive study should be carried out to isolate and identify the bacillus and perform drug sensitivity tests. The appropriateness of the treatment depends on all this and the survival of patients with minimal neurological sequelae depends on it.
PERI-IMPLANT POTT'S SPINE IN AN OPERATED CASE OF BURST FRACTURE: A RARE CASE REPORT

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Background and Aims:: Short segment pedicle screw fixation is a standard of treatment for Lumbar burst fractures. Isolated case reports have been published on tubercular infection of bone and joints following fracture fixation surgery, but no report is available on tubercular infection of the adjacent vertebra following pedicle screw fixation.

Methods:: 27-year-old female was diagnosed with L1 burst fracture without any neurological deficits following a road traffic accident and was operated with posterior pedicle screw fixation from D12 to L2. Post-operatively patient was asymptomatic for 5.5 years after which she started complaining of lower back ache which was insidious in onset, non-radiating and gradually progressive. There were no constitutional symptoms or deficits. On radiographic evaluation there was collapse at L2-L3 level with T1 hypointense and T2 hyperintense marrow, edema and collection. Diagnosis of late infection was made with the possibilities being pyogenic or tubercular infection. Percutaneous pedicle biopsy was taken from L3 vertebrae and was sent for histopathology, Culture sensitivity and Cartridge based nucleic acid amplification test (CBNAAT) for tubercular infection. Histology revealed tubercular epitheloid granulomas and CBNAAT was positive for mycobacterium tuberculosis.

Results:: Patient was put on Anti-tubercular therapy (ATT) with two months of Isoniazid, rifampicin, ethambutol and pyrazinamide (HRZE) and 16 months of HRE with regular follow-up. Pain settled within two months after onset of therapy. At the end of ATT course patient was planned for implant removal surgery and did not need any stabilisation and healed with a kyphosis of <20 degrees.

Conclusions:: The distinct possibility of tubercular infection should always be kept in spondylodiscitis infections and conservative management with ATT yields good results when residual kyphosis is not significant.
COMPARISON OF PATTERN OF INFACTIONS IN TUBERCULOUS AND CRYPTOCOCCAL MENINGITIS

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Background and Aims:: To compare the frequency and pattern of stroke, the specificity of tubercular zone (TBZ) infarction and its effect on outcome in tuberculous (TBM) and cryptococcal meningitis (CM).

Methods:: This retrospective study was conducted at two tertiary centres in India during May 2018 to Jul 2020. Sixty-one patients with TBM and 22 with CM were included. The primary outcome was proportion of patients of TBM and CM with infarction. Secondary outcomes included anatomical locations of infarction and in-hospital mortality.

Results:: Infarctions were noted in 52.5% of patients with TBM and 54.5% in CM (P = 0.87) with caudate head infarcts in 9.4% vs 41.7% (P=0.01), cerebellar in 9.4% vs 33.3% (P=0.05), thalamic in 25% vs 0 and lobar in 28.1% vs 0 respectively. In TBM, the infarcts were located in TBZ in 3 (9.4%), ischemic zone (IZ) in 23 (71.9%), with six (18.8%) patients showed infarcts in both, while in CM group, it was in 0 (0%), 6 (50%) and 6 (50%) patients respectively. Infarcts were not associated with in-hospital mortality neither in TBM nor CM.

Conclusions:: Caudate head and cerebellar infarctions were more common in CM, while, thalamic, and lobar infarcts were frequent in TBM. TBZ infarcts were not specific to TBM.
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VANISHING CEREBRAL RING ENHANCING LESIONS; A THREE YEAR MYSTERY

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Background and Aims:: Vanishing tumor is a rare phenomenon where the tumor spontaneously disappears or reduces to less than 70% of the initial volume without definitive treatment. We revisit the diagnosis of a patient initially diagnosed with cerebral metastases of unknown primary whose lesions vanished after three years.

Methods:: Case report A 44 year old woman presented with subacute onset hemiparesis, confusion and focal seizures. The presence of multiple haemorrhagic ring enhancing lesions (figure 1) prompted a diagnosis of cerebral metastases. Extensive workup failed to reveal a primary neoplasm and unfortunately she did not receive specific treatment and defaulted follow up. Three years later during evaluation for uveitis (figure 2) the cerebral lesions were found to have disappeared (figure 3). Cerebrospinal fluid analysis was normal. Investigations excluded sarcoidosis and tuberculosis. Further questioning uncovered a history of parotitis and contact with cats. Toxoplasma IgG was positive in serum and a diagnosis of toxoplasmosis was made. She was non-diabetic and immunodeficiency screening including HIV was negative.
Results:: Discussion Vanishing cerebral lesions pose a diagnostic dilemma. Differential diagnosis includes primary CNS lymphoma, inflammation, demyelination, neurosarcoidosis, and infection. As biopsy is often deferred due to operative risks, a careful history and patient follow up is paramount. Eccentric target sign (figure 1) is characteristically seen in cerebral toxoplasmosis with a specificity of 95%. Although there have been reports of cerebral toxoplasmosis in immunocompetant patients, an underlying immunodeficiency state should always be considered.

Conclusions:: Cerebral toxoplasmosis can lead to vanishing brain lesions. This diagnosis is supported by pathognomonic neuroradiological findings and serology.
Background and Aims:: Neurocysticercosis (NC) is one of the main parasitological diseases affecting the central nervous system. It is a disease linked to poverty and is considered endemic in most countries in Asia, Sub-Saharan Africa, and Latin-America. The evaluation of its frequency in endemic countries is difficult to carry out since there are no systematic records. In this context, the evaluation of the frequency of hospitalization represents information of interest. The objective of this work was to evaluate the evolution of the frequency of hospitalization of patients with NC between 1995 and 2019, at the Manuel Velasco Suarez National Institute of Neurology and Neurosurgery (INNN).

Methods:: The data were obtained from the hospital epidemiology service, using ICD-10 coding B.69. We complement this information with the hospital discharge data from the different public care institutions between 2004 and 2019. The index of NC hospitalizations/total hospitalizations was obtained for each service. The public care institution's information was obtained from national records and an official health secretary website.

Results:: In the INNN, the frequency of hospitalization decreased significantly in neurosurgery (R = -0.69; p <0.001) and in neurology (R = -0.68; p = 0.001).

The analysis of hospital discharges from the public institutions in the country showed the same trend. (R = -0.978; P<0.0001).
The average age of the patients increased significantly during the period of study ($R = 0.77; p < 0.001$).

**Conclusions:** These results are very encouraging, probably related to the improvement of hygienic-sanitary conditions in rural areas. However, although less frequent, the disease persists. Efforts to achieve eradication must continue.
PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY AFTER IMMUNOCHEMOTHERAPY WITH DRD PROTOCOL FOR MULTIPLE MYELOMA: A CASE REPORT

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Background and Aims:: A 65-years-old woman with a refractory Multiple Myeloma (MM) treated with Daratumumab in combination with Lenalidomide and Dexamethasone (DRd) was admitted to our Neurology Unit for the subacute onset of left upper limb weakness, ataxia, and dysarthria.

Methods:: As differential diagnosis, we considered: infective CNS diseases, cerebrovascular disease, chemotherapy- related encephalopathy and autoimmune or paraneoplastic syndromes. In order to make the correct diagnosis we performed a diagnostic procedure, including brain and spinal cord MRI, blood tests and CSF analysis.

Results:: MRI findings showed multiple diffuse white matter (WM) T2/FLAIR hyperintensities localized in the central pons and bilateral cerebellar peduncles and white matter, with diffusion restriction at the edges of the lesions. CSF analysis was positive for the presence of JC virus DNA (942 copies/mL), whereas all other microbiological investigations were negative. Blood laboratory tests showed the presence of JCV DNA on plasma (1020 copies/mL). Taken together these findings supported the diagnosis of progressive multifocal leukoencephalopathy (PML) secondary to a profound and combined immunodeficiency attributable to both the MM and the immunochemotherapy.

Conclusions:: PML is a life-threatening demyelinating CNS disorder caused by JC virus reactivation. To the best of our knowledge, there are only few other reports on PML occurring in association with Daratumumab therapy. Moreover, MRI findings of this case were relatively uncommon since demyelinated areas were exclusively and extensively located in the brainstem and cerebellar areas. Further studies are required to assess a causal relationship between Daratumumab and PML.
THE UNAVERTED COEXISTENCE OF MENINGEAL AND SPINAL TUBERCULOSIS, A SERIES OF CASES

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Background and Aims:: Tuberculosis is a public health problem with high mortality. Central nervous system affection represents 2% of all cases, it can affect intracranial or spinal structures. The association of meningeal and spinal infection is infrequent, being associated with a poor prognosis.

Methods:: A retrospective study was carried out in a cohort of patients with meningitis tuberculosis associated with spinal tuberculosis treated from January 2013 to February 2021.

Results:: There were 22 patients with both, meningeal and vertebral tuberculosis, the risk factors were HIV infection 27.27% and diabetes mellitus 22.72%; and 45.45% remained without risk factors. The initial symptoms were fever in 77.27%; headache 72.72%; weight loss 63.63%; 27.27% presented paraplegia and 18.18% paraparesis. The results obtained from the CSF study and the MRI established the final diagnosis. The CSF study showed pleocytosis 40.90%, hyperproteinorachia 50%, with a mean of ADA of the 19.07 U / L, 31.81% showed a positive Lowestein Jensen culture, 27.23% GeneXpert +. The MRI of the skull and spinal showed leptomeningitis 28.6%, tuberculomas 28.6%, and arachnoiditis 28.6%; hydrocephalus and vasculitis in 21.4%, spondylodiscitis 57.1%, vertebral collapse 35.7%, paravertebral abscess 35.7%, and spinal tuberculomas 21.4% of the patients.

Conclusions:: The association of meningeal and vertebral tuberculosis should be suspected in every patient who presents fever, weight loss and gait alteration associated with comorbidity such as HIV and diabetes. Some cases require drainage of the paravertebral abscess and spinal cord decompression. If a rapid diagnosis and treatment is not accomplished, the risk of complications, disability and death increases.
GEOPHAGY AS RISK BEHAVIOUR FOR NEUROCYSTICERCOSIS AMONG CONGOLESE WOMEN

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Background and Aims:: Neurocysticercosis (NCC) is a common helminthic infection of the nervous system that occurs when humans become intermediate hosts in the life cycle of the pork tapeworm, Taenia solium, after ingesting its eggs. The disease is most often transmitted by tapeworms to healthy individuals through unhygienic handling or direct contact with human excreta. Clay (Pemba) consumption soiled by Taenia solium eggs can cause NCC. This study aims to describe socio-demographic, clinical, and neuroimaging features of patients with NCC related to geophagy or consumption of clay in our environment.

Methods:: This is a cross-sectional descriptive study, carried out in Lubumbashi in the Democratic Republic of Congo, from January 2019 to June 2020. For each patient examined, we collected socio-demographic, clinical and neuroimaging features, and therapeutic modalities.

Results:: We examined 6 patients, all of whom were female, with a mean age of 27.5 years (range: 23-37 years). Contact with pork was noted in 5 patients (83.3%), all patients regularly consumed clay (100%). Generalized epilepsy was observed in 66.6%. In neuroimaging, first stage lesions were found in 3 patients, third stage lesions in 2 patients, and fourth stage lesions in 5 patients. In 2 patients, 2nd, 3rd and 4th stage lesions were noted simultaneously. Frontal location of lesions was the most found (100%), followed by parietal location (66.6%). Three patients (50%) had more than 10 lesions. All patients evolved well under antiepileptic drugs alone or associated with antiparasitic treatment.

Conclusions:: This study shows that geophagy is also a risk behavior of neurocysticercosis found in our environment.
CRYPTOCOCCAL MENINGITIS: DIAGNOSTIC AND THERAPEUTIC CHALLENGE IN PLACES WITH SCARCE RESOURCES.

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**Background and Aims:** A 34 years old male, HIV positive diagnosed 2 months ago during hospitalization due to bifrontal hemorrhage contusion after cranioencefalic trauma, in antiretroviral treatment with TDF-3TC-DTG, hospitalized with generalized clonic tonic convulsions, severe headache and behavior change characterized by incoherent speech. Neurological examination: with slower speech, depressed mood, facial acymetry with deviation of the right lip commissure; gait unevaluable, patient prostrate and not sitting without support, muscular strength 3/5 in the left hemibody, right lower limb with 4/5. with stiff neck and positive Kernig signal. General physical examination: fever temp: 38,5 celsius, extreme cachexia, with decubitus bedsores in the buttocks and calcaneus. skin with several insignia of traditional treatment.

**Methods:** case report

**Results:** CBC: WBC: 4,45; HB: 10.9; linf: 15,3%; Neutrof: 73.8% VHS: 52mm/H Biochemistry: normal CSF cytochemistry: Yeasts are observed, glucose- 0.22 Anti-toxoplasmosis antibody: non-reactive IgG / IgM

**Conclusions:** Definitive diagnosis: Cryptococcal meningitis; AIDS AIDS IV Specific Treatment instituted: Amphotericin B 50mg / day ev; Fluconazole 1200mg / d Antiretroviral Treatment Others treatments: Cotrimoxazol 960mg/d, Ceftriaxone 2g 12/12h; hidratation, analgesics. With current difficulties due to the absence of imaging exams like TAC and NMR, and ideal treatments options, the diagnosis of CNS infections has been a huge challenge, but we strive for the best for patients.
NEUROCOGNITIVE IMPAIRMENT AND EPILEPSY IN SCHOOL-AGED CHILDREN AFTER SEVERE MALARIA IN A MALARIA ENDEMIC AREA.

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Background and Aims: Severe malaria is a contributor to neurocognitive impairment and epilepsy in children living in sub-Saharan Africa but there is no published data on this subject in Cameroon. We thus sought to understand the possible neurological long term effects of severe malaria in school-aged children in Yaoundé.

Methods: In this retrospective cohort study of 50 eligible children who survived severe malaria in Yaoundé, demographic, clinical, neuropsychological and electroencephalographic evaluations were done using standard clinical procedures.

Results: The mean age was 9.38±3.06 years. The prevalence of neurocognitive impairment and epilepsy were 38% and 20% respectively. The risk of developing epilepsy evaluated by EEG epileptic activity was 34.4%. The incidence of neurocognitive impairment was 226 cases per 1000 person years. The incidence of epilepsy and epileptic activity on the electroencephalogram were 140 and 154 cases per 1000 person years respectively. The most affected cognitive domains were: fine motor skills, sustained attention, mental flexibility and verbal memory. There was no association between coma and neurocognitive impairment (p=0.54) but there was an association between high daily seizure frequency during malaria and subsequent epilepsy (p=0.013 respectively) and between disease duration and epileptic activity (p=0.043).

Conclusions: The prevalence and incidence rates of neurocognitive impairment and epileptic activity are significantly high in children who suffered from severe malaria in Yaoundé. High seizure frequency during severe malaria appears to be a predictor of epilepsy while coma is not a predictor of neurocognitive impairment in these children.
CHRONIC PAIN AMONGST HIV-INFECTED ADULTS FOLLOWED-UP AT THE BAMENDA REGIONAL HOSPITAL, CAMEROON

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Background and Aims:: Pain has been recognised as a common symptom people living with HIV. The prevalence ranges from 24% amongst ambulatory patients, 50%-60% in hospitalised patients and 60%-70% in hospice settings. Severe pain can potentially impact in quality of life and functional ability. Little is known on the prevalence of pain and associated factors in Cameroonian population of people living with HIV, hence the study.

Methods:: This was an observational cross-sectional study involving HIV-infected adults followed-up at the Bamenda Regional Hospital. Data were collected on demographics, baseline HIV information and on pain. Research tools included the Brief pain inventory short form, the patient health questionnaire-2 and the self-administered Leeds assessment for neuropathic symptoms and signs.

Results:: A total of 290 participants completed the questionnaire of which 71.0% were female. The mean age was 47.47 (SD11.047). Almost 90% were adherent to combined antiretroviral therapy and 37.2% had been on treatment for 11 – 15 years. The prevalence of chronic pain was 27.6% with musculoskeletal (22.5%) and neuropathic (65%) pain being the most common. Pain most severely interfered with walking ability. None of the factors analysed including, age, gender or adherence to combined antiretroviral therapy, were significantly associated with chronic pain (p=0.224 95% CI 0.151 – 0.242 for non-adherence to p=0.847 95% CI 0.990 – 1.000 for gender).

Conclusions:: Pain is common in this population with HIV with musculoskeletal pain being the most prevalent. None of the factors analysed including age, gender or adherence to combined antiretroviral therapy were significantly associated with chronic pain.
NEUROLOGICAL OPPORTUNISTIC INFECTIONS AND WHY WE SHOULD NOT RELY ON CD4+ THRESHOLDS - A REPORT OF TWO CASES OF HIV-INFECTED PATIENTS WITH CNS DISEASE.

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Background and Aims:: CD4+ T-cell count (CD4+) has guided the diagnostic assumptions on HIV-infected patients with neurological disease. However, evidence has revealed the incidence of neurological opportunistic infections despite CD4+ > 200 cells/mm³. Aim: to describe two cases of CNS opportunistic infections in patients with CD4+ over the risk ranges.

Methods:: Case study.

Results:: Patient 1: A 46-year-old man with HIV infection presented with cognitive impairment, tremor, and fecal incontinence over the past few months. His CD4+ was 464 cells/mm³ and he was under treatment with ART. He had been treated for cerebral toxoplasmosis one year prior - his CD4+ was 18 cells/mm³ then. Neurological examination disclosed parkinsonian symptoms and slowed thought processes. A brain MRI showed bilateral T1 gadolinium-enhanced lesions in the basal ganglia. He was diagnosed with cerebral toxoplasmosis and had a marked improvement after pyrimethamine, sulfadiazine, and leucovorin therapy.
Patient 2: A 31-year-old man with HIV/AIDS poorly adherent to the treatment with ART presented with recurrent seizures and acute left hemiplegia. His CD4$^+$ was 258 cells/mm$^3$. Seven months before, he had been treated for cryptococcal meningitis - with a CD4$^+$ nadir of 64 cells/mm$^3$. Head CT showed large hypodense areas in the right frontal and parietal regions. CSF was positive for JC virus on polymerase chain reaction. He was diagnosed with progressive multifocal leukoencephalopathy. The ART was adjusted then and the clinical condition remained stable.
Conclusions: CNS opportunistic infections should be suspected in patients with HIV/AIDS and medical history of severe immunosuppression, even if they have partially recovered the CD4+.
INCIDENCE OF TICK-BORNE ENCEPHALITIS IN THE REPUBLIC OF BASHKORTOSTAN (RUSSIA) IN XXI CENTURY

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Background and Aims:: Tick-borne encephalitis (TBE) is transmissive zoonotic disease often severely affecting nervous system. A number of studies conducted in different geographical areas demonstrated evolution of TBE. Official registration of the cases of TBE in the Republic of Bashkortostan started approximately 70 years ago. Aim. To assess the main clinical and epidemiological features of TBE in XXI century and compare them with the data registered in XX century.

Methods:: We analyzed clinical and epidemiological features of 736 cases of TBE in the Republic of Bashkortostan starting from 2000. The comparative analysis with the data registered in XX century was performed (data in brackets).

Results:: The overall incidence of TBE in 2000-s was 0,91±0,45 cases per 100 000. In comparison to 1970-90-s this parameter decreased 3 times (3,05±1,12).Mean incidence mostly decreased in the Cis-Urals region while the majority of cases of TBE with clinical manifestation occurred in South Urals region of the Republic of Bashkortostan. The proportion of people who contracted TBE during outdoor recreational activities increased (р<0,05) and reached 40,46±12,60% (28,22±8,36%).

Conclusions:: 1) The incidence of TBE in the Republic of Bashkortostan in XXI century in comparison to 1970-90-s (р<0,05) decreased down to 0,91±0,45 cases per 100 000 people. 2) The frequency of the cases of TBE contracted during the outdoors recreational activities increased (р<0,05) up to 40,46±12,60% in XXI century, in comparison to XX century.
PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY RELATED TO HIV1 INFECTION WITHOUT CELLULAR IMMUNODEFICIENCY: CASE REPORT

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Background and Aims:: Progressive Multifocal Leukoencephalopathy (PML) is a rare and debilitating disease of Central Nervous System (CNS) caused by JC virus (JCV), a poliomavirus generally located in CNS as asymptomatic infection in general population. In immunosuppressed patients, JCV can induce progressive damage of oligodendrocytes. We describe a patient with HIV1–related PML that occurred despite undetectable impairment of cellular immunity.

Methods:: Case report:A 42-years-old male came to our attention with a ten-months history of progressive vision loss and limbs tremor. His past medical history included HIV1 infection since 28-years old, treated with antiretroviral therapy. At admission, neurological examination showed bilateral ipovision, dysarthria, dysmetria, ataxia, mixed tremor at four limbs. Serum HIV load was 20700 copies/ml with normal CD4+ cell count. Brain MRI showed bilateral T2–weighted hypertintense lesions in cortical and subcortical parieto-occipital lobes; post-gadolinium T1-weighted images showed punctate foci of enhancement (milky way sign) in cerebellar hemispheres, basal ganglia and ribbon-like enhancement of U-fibers in fronto-parietal lobes. CSF PCR detected JVC and confirmed the diagnosis of PML. Empiric treatment with mirtazapine and short course of high dose steroids was started, but despite these treatments the patient’s neurological condition worsened and he died 5 months after diagnosis.

Results:: In the present case, PML was related to HIV1 infection with absence of any serological sign of immunosuppression.

Conclusions:: Very rarely PML was reported in apparently immunocompetent patients assuming these clinical cases may have undetectable immunodeficiency at the stage of diagnosis.
COMPLEX THERAPY OF NEUROLOGICAL SYNDROMES IN HIV INFECTED PATIENTS

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Background and Aims:: The aim of the study was to optimization of pathogenetically based approach to complex therapy of major neurological syndromes in HIV patients.

Methods:: The study is based on the survey data of 73 patients with HIV infection (54.4% women and 45.6% men), aged from 20 to 45 years old. For neuropsychological studies used Wechsler Memory Scale (WMS), "Schulte tables" and "Incomplete contours of objects" (AR Luria). The citicoline (1000 mg/day) added to the basic HIV therapy, was studied in 38 patients. The comparison group consisted of 35 HIV patients who did not receive neuroprotective therapy. The effectiveness of treatment was assessed using the clinical scale CGI (Clinical Global Impression).

Results:: In the main group, despite the therapy, deterioration was not noted. After treatment, there was significant increase in the mean equivalent memory indices (EMI) (96.8 ± 2.5 versus 112.6 ± 3.8; P <0.05). In the comparison group, there is also a tendency to an increase in the average EMI values, before treatment was 8 (22.8%) of cases, then after treatment it is increased by 5.7% (P> 0.05), while in the main group consisted of 12 (31.5%) patients. In 18 (47.3%) patients of main group showed expressed improvement, and in 20 (52.7%) had a moderate improvement. In comparison group of patients were expressed, moderate, improvement and without improvement observed in 11 (31.4%), 17 (48.5%), 4 (11.4%) and 3 (8.7%), respectively.

Conclusions:: The present study has demonstrated the effectiveness of citicoline ("ceraxone") in the treatment of neurological disorders in patients with HIV.
Background and Aims:: Neuromeningeal cryptococcosis (NMC) is a most common opportunistic fungal disease in people living with HIV/AIDS (PLWHA). This infection is caused by Cryptococcus neoformans, a yeast-fungus, encapsulated, cosmopolitan and living in several ecological niches very frequent in Africa because of climatic and ecological conditions. This study aims to describe the sociodemographic, clinical, and outcome features of NMC among PLWHA in Lubumbashi in the Democratic Republic of Congo.

Methods:: This is a retrospective study of 108 cases of NMC diagnosed in PLWHA. Data are collected for 3 years (from January 2015 to December 2017) at HIV / AIDS Center of Excellence in Lubumbashi. Variables studied were age, gender, clinical, biological, therapeutic, and outcome features.

Results:: The overall prevalence of NMC was 2.5%. The mean age was 41.5 ± 13.1 years old, with 72.2% of patients aged less than 50 years. The main clinical symptomatology was headache (100%) and fever (100%). The main cytochemical abnormalities of cerebrospinal fluid analysis were hyperproteinorachy (91.9%), hypoglycorachy (94%) and lymphocytosis (98.2%). The mean CD4 cell count was 168.7/mm$^3$. Patients were initially treated with fluconazole. The overall mortality was 43.5%.

Conclusions:: NMC is a serious opportunistic infection in PLWHA, and the mortality rate remains unacceptable. Fighting NMC in PLWHA requires early diagnosis, increased access to antiretrovirals, rapid introduction of appropriate treatment.
TOCILIZUMAB AS STEROID-SPARING AGENT FOR POST-INFECTIOUS INFLAMMATORY RESPONSE SYNDROME IN TWO NON-HIV CRYPTOCOCCAL MENINGITIS PATIENTS

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Background and Aims:: Non-HIV Cryptococcal Meningitis (CM) is often complicated by a post-infectious inflammatory response syndrome (PIIRS), characterized by neurologic deterioration in previously-healthy patients with CM after appropriate antifungal therapy and conversion of CSF fungal cultures to negative. PIIRS is due to an appropriate inflammatory response to fungal antigen released during therapy, mediated by IFN-gamma and IL-6 stimulating T-helper cells, leading to immune-mediated host damage. At the National Institutes of Health (NIH), patients with non-HIV CM-related PIIRS have been successfully treated with methylprednisolone burst and slow prednisone taper. However, occasional patients will be refractory to steroid therapy, unable to be weaned from high-dose steroid, or require prolonged periods of high-dose corticosteroids that may have problematic side-effects. Hence, appropriate steroid-sparing agents are needed in the treatment of refractory PIIRS. Due to the role of IL-6 in its pathogenesis, IL-6 receptor blockade by tocilizumab is of interest in the treatment of PIIRS.

Methods:: Two previously healthy patients with non-HIV CM-related PIIRS who were steroid-refractory were seen at the NIH. Due to intractable symptoms (Patient A with refractory headaches and elevated intracranial pressures despite VP-shunt, and Patient B with persistent altered mental status), and ongoing evidence of CSF inflammation, both patients were treated with monthly tocilizumab infusions.

Results:: Both patients exhibited rapid symptomatic improvement, permitting steroid taper. Patient A had near resolution of headaches. Patient B showed mental status improvement as evidenced by improved MOCA score. Both had improved CSF parameters, and no significant side-effects.

Conclusions:: Tocilizumab may be a safe and effective treatment for steroid-refractory non-HIV CM-related PIIRS.
Background and Aims:: Neurosyphilis is a great imitator and has varied presentations. We report a case presenting as corticobasal syndrome and its atypical MRI findings are described.

Methods:: Descriptive Case report of rare clinical presentation and MRI findings of Neurosyphilis

Results:: A 65 year old male presented with progressive cognitive decline of 2 years duration. There was associated slowness and posturing of left hand. He worsened over time and became partially dependent for activities of daily life. On examination he had nonfluent aphasia, executive dysfunction, ideomotor, dressing and constructional apraxia, visuospatial deficits, asymmetric parkinsonism (left more), left hand dystonia and cortical sensory deficits. MRI Brain showed right parietal T2 FLAIR hyperintensity with curvilinear blooming artifacts. Curvilinear cortical blooming artifacts were also seen over bilateral temporal, frontal, occipital and left parietal areas. There was parenchymal atrophy as well as small vessel ischemic changes. Serum VDRL and TPHA were positive and HIV was negative. EEG showed mild theta slowing. CSF evaluation showed lymphocytic pleocytosis (20/mm3), mild protein elevation (55mg/dL) and positive CSF VDRL. Serum paraneoplastic antibody panel, anti thyroperoxidase antibody and CSF autoimmune antibody panel were negative. A diagnosis of Neurosyphilis was made and he was treated with benzylpenicillin 4 MU fourth hourly for 2 weeks. Symptomatic treatment was given with levodopa-carbidopa, memantine and donepezil.

Conclusions:: Neurosyphilis is a great imitator. Corticobasal syndrome is a rare presentation of Neurosyphilis. Susceptibility weighted images showing cortical blooming may point towards neurosyphilis. High index of suspicion is needed to diagnose neurosyphilis and CSF VDRL examination should be part of dementia workup.
Background and Aims:: In Tuberculosis/COVID 19 co-infection, successive inflammatory stimuli lead to depletion of T cells. The resulting lymphopenia affects the immune response against pathogens. This co-infection can have secondary effects such as a greater expression of the ACE2 receptor on the cell surface stimulated by IFN, IL4, IL13, with greater immunopathological damage. Both entities are transmitted by air and mainly affect the lungs, they can also affect other organs and have similar symptoms, which makes the diagnosis of this co-infection difficult.

Methods:: presented two cases

Results:: We present 2 clinical cases: the first is a 17 year old male, without risk factors, admitted for fever, headache, nausea, vomiting, weight loss, cough, and disabling bone pain in the lumbar and cervical spine. Chest X-ray with bilateral nodules, pneumonia and mediastinal widening, positive PCR test for SARS-CoV2. Due to bleeding from the lower digestive tract, he was taken to surgery, finding intestinal and peritoneal tuberculosis. MRI of the neuroaxis revealed meningeal tuberculosis and paravertebral abscesses in the cervical and lumbar spine. The second case is a 24 year old male, HIV +, with a history of splenectomy due to thrombocytopenic purpura, and consumption of unpasteurized dairy products. Both men had cough, dyspnea, and hypoxemia, and required intubation. Their neurological manifestations were headache; seizures; hallucinations; cognitive, sensory and motor deficits; and sphincter disorders. M. bovis was isolated in the CSF, gastric juice, expectoration and urine, the first patient had tuberculosis in 7 organs.

Conclusions:: Both of them survived the SARS-CoV2 infection and continued to be treated for tuberculosis.
HEPATITIS E INDUCED BRACHIAL PLEXITIS

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Background and Aims:: A 57 years old heavy vehicle driver had sudden onset shooting pain in the left upper limb that spread to the other side. He also noticed anaesthesia of both his upper limbs. He had difficulties in lifting his arms above the shoulder. He also had exertional breathlessness. He had significant motor weakness of his upper limbs. Reflexes were absent in the upper limbs. He had no clear sensory abnormality or cerebellar signs. He was tachypnoeic. Hepatitis E IgM came back as positive. His hepatitis E RNA showed 1810 RNA units. The nerve conduction and EMG help us get the diagnosis as bilateral brachial neuritis associated with an acute HEV infection. Six weeks later, he returned with worsening orthopnea. He had paradoxical abdominal movements while lying flat. He developed bilateral diaphragmatic paresis during the sniff test. The chest X ray revealed that the domes of diaphragm were at the same level. He was discharged with non-Invasive ventilation.

Methods:: Retrospective analysis of a rare case
Results:: Hep E is an important cause of Brachial neuritis
Conclusions:: The brachial neuritis associated with an acute HEV infection is often bilateral and severe. Such plexopathy usually affects middle-aged men, like our patient. Bilateral phrenic paralysis was reported in less than 1% patients with idiopathic brachial neuritis. [4] The involvement of the phrenic nerve with diaphragmatic weakness is more common than brachial neuritis with HEV infection. [2] The prognosis of brachial neuritis associated with HEV infection is often unfavourable because of severe bilateral involvement of the brachial plexus and diaphragm. Recovery is often incomplete.
A CORRELATIVE STUDY OF THE INCIDENCES OF ACUTE GUILAIN-BARRÉ SYNDROME AND VIRAL MENINGOENCEPHALITIS IN ADULT PATIENTS AT BENGHAZI MEDICAL CENTER DURING 2019 (PRE COVID 19)

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Background and Aims:: Viral diseases cause meningoencephalitis VME. Associated GBS is recognised. We aimed to study the correlation between the incidences of GBS and VME, in adult patients admitted to Benghazi Medical Center BMC, from 1st January 2019 to 31st December 2019.

Methods:: A retrospective study reviewing the files of patients admitted to BMC diagnosed with acute GBS and or VME.

Results:: From a total of 226 neurological admissions, 28 Libyan patients had the conditions: GBS 26 cases, VME 3 cases, GBS and VME 1 case. Males: 13, Females 15. The GBS age range was: 17-86 years. VME occurred at ages 24-45 years. The incidence of GBS in 2019 was 2.6/100,000. Acute inflammatory demyelinating polyneuropathy AIDP frequency was 63.2%, and axonal types 21.1%. 57.1% received IVIG, 39% plasma exchange, and 17.9% both. The incidence of VME in 2019 was 0.3/100,000 population. No mortalities were recorded.

Conclusions:: For a population of one million we found an annual incidence of GBS of 2.6/100,000, similar to other countries pre COVID 19. We found a wide age range for GBS. The most frequent GBS types were AIDP, followed by the axonal type, similar to other countries. VME was less frequent but correlated with the first half of the year rises in GBS. A peak of GBS in May, a case appearing to have both conditions, correlated with the recognised aetiology of GBS. GBS also peaked in winter. Both conditions increased in August, consistent with others, increasing in the hotter months. We found similar peaks recorded for COVID 19 during 2020.
DIAGNOSTIC ACCURACY OF THE FILMARRAY™ MENINGITIS/ENCEPHALITIS PANEL IN ADULT PATIENTS WITH SUSPECTED BACTERIAL MENINGITIS IN A TERTIARY CARE HOSPITAL IN THE PHILIPPINES

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Background and Aims:: Bacterial meningitis is associated with significant morbidity and mortality if not diagnosed and treated early. Isolation of the causative agent from cerebrospinal fluid culture is the gold standard for the diagnosis of this condition; however, it takes several days for results to be available. The FilmArray™ Meningitis/Encephalitis (ME) panel is a nucleic acid-based test that allows simultaneous detection of 14 bacterial, viral, and fungal pathogens in the cerebrospinal fluid with a rapid turnaround time. Our aim was to evaluate the diagnostic performance of the ME panel in detecting bacterial pathogens in the cerebrospinal fluid of adult patients with suspected bacterial meningitis.

Methods:: We performed a retrospective review of hospital records of adult patients with suspected bacterial meningitis who were admitted at a tertiary care hospital in the Philippines and underwent diagnostic testing with the FilmArray™ Meningitis/Encephalitis (ME) panel from January 1, 2018 to July 31, 2019. Overall percent agreement, sensitivity, and specificity for individual bacterial pathogens included in the panel were determined.

Results:: A total of 98 patients were included in the analysis. The ME panel demonstrated 98% overall agreement, 50% sensitivity, and 99% specificity in comparison with CSF culture in detecting bacterial pathogens in the cerebrospinal fluid.

Conclusions:: The results show that the FilmArray™ Meningitis/Encephalitis panel has high diagnostic accuracy and can be utilized in the rapid diagnosis and targeted treatment of patients with bacterial meningitis, aid antimicrobial stewardship, and improved patient outcomes.
HUMAN HERPES VIRUS 6 ENCEPHALITIS PRESENTING AS FATAL REFRACTORY STATUS EPILEPTICUS: A CASE REPORT AND SYSTEMATIC REVIEW

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Background and Aims:: Encephalitis secondary to human herpesvirus 6 (HHV-6) infection is frequently detected in immunocompromised patients; in contrast, HHV-6 encephalitis in immunocompetent patients is rare. We report a case of a previously healthy 46-year-old female with HHV-6 encephalitis who presented with status epilepticus unresponsive to multiple antiepileptic medications.

Methods:: Case Report

Results:: Our patient is a 46-year-old female who presented with a one-week history of back pain, fever and generalized tonic-clonic seizures that progressed to status epilepticus. The video electroencephalography showed epileptiform discharges on both frontotemporal regions. Neuroimaging showed hyperintensities on the bilateral insula and temporal lobes. Lumbar puncture was performed and the cerebrospinal fluid showed elevated pressure. The CSF was tested using the FilmArray Meningitis/Encephalitis panel and was positive for HHV-6. She was given ganciclovir and a total of eleven antiepileptic drugs. Despite these medications, she developed refractory status epilepticus and eventually succumbed due to multiple medical complications.

Conclusions:: Our case highlights HHV-6 encephalitis as an important diagnostic consideration in patients with refractory status epilepticus, regardless of immune status.
Background and Aims:: Introduction: Intracranial tuberculous abscess is a less common form of tuberculosis, accounting 0.15 to 4 percent of extrapulmonary tuberculosis. Furthermore, involvement of the sellar area is one of the rarest location, with only few cases documented in the literature. This case reported a 38-year-old male who presented with chronic headache. He was clinically diagnosed and treated as a case of tuberculous meningitis (TBM), however, a cranial magnetic resonance imaging with contrast showed a sellar mass which was initially diagnosed as pituitary macroadenoma and not a sequela of TBM; with the expansile mass effect, he had new-onset bilateral hemianopia and pituitary function panel revealed central hypothyroidism and secondary adrenal insufficiency. Objective: This case report aims to identify the clinical implication of considering tuberculous abscess as differential diagnosis in the setting of a cystic sellar mass.

Methods:: An endoscopic endonasal trans-sphenoidal surgery with complete drainage of caseous material in the pituitary fossa was performed. The finding was consistent with pituitary tuberculous abscess.

Results:: The symptoms significantly resolved after drainage and antibiotic therapy, with resolution of hypothyroidism and adrenal insufficiency.

Conclusions:: Pituitary tuberculous abscess is rare. A high index of suspicion for a prompt combination of medical and surgical treatment of this condition is important to prevent the development of life-threatening complications.
SUBAIGUE SCLEROSANTE PANENCEPHALITIS: MRI BENEFITS STUDY OF 8 CASES OBSERVED IN A TROPICAL ENVIRONMENT

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Background and Aims:: the goal of a reassessment of this pathology from a clinical and evolutionary point of view. The interest of this work lies in the fact that these observations are a good illustration of subacute sclerosing panencephalitis and the difficulty of differential diagnosis that it entails with neurodegenerative disorders with myoclonic and epileptic connotations in tropical settings.

Methods:: eight (8) patients were evaluated retrospectively over a period of January 1, 2012 to December 31, 2019. The diagnostic approach was based on clinical data: progressive mental deterioration myoclonus, ophthalmologic abnormalities, specific electroencephalographs and cerebrospinal fluid abnormalities and neuroradiological aspects. The differential diagnosis of subacute sclerosing panencephalitis can arise with other conditions, in particular the myoclonic syndromes observed in neurodegenerative conditions and the various encephalic infections common in tropical settings.

Results:: an infectious clinical picture without vaccination was identified in 14 patients and only 4 patients had a record notifying vaccination with measles. The clinical signs were summarized as the existence of a clinical headache with severe cognitive deterioration due to the under-medicalization and ophthalmologic abnormalities observed in patients. The disease virus IgG and IgM laboratory tests were instrumental in the diagnosis.

Conclusions:: this study shows the presence of Subacute sclerosing panencephalitis and requires increased prevention by vaccination.
VARICELLA ZOSTER ENCEPHALITIS: SPREAD SPECTRUM

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Background and Aims:: Varicella Zoster Virus (VZV) is a human neurotropic virus. The primary infection causes varicela (chickenpox), and then, the virus remains latent in the sensory cranial neurons or dorsal root ganglia. VVZ can be reactivated in elderly (age older than 50 years) or immunodepressed patients, causing herpes zoster, vasculopathy, meningoencephalitis, meningoradiculitis, cerebellitis, myelopathy and ocular disease.

Methods:: We present two case reports with diagnosis of VZV meningo-encephalitis.

Results::

CASE A. 87-years-old woman, without relevant medical history, who presented jerks in left extremities and language alteration. In the emergency room, we activated stroke code, with normal neuroimaging studies. After this, she presented comatose state and ocular robbing, and some hours later she started to present psicomotor agitation. We performed a lumbar puncture, with leucorrhachia (mononuclear prevalence). MRI was normal. There were no fever, rash, increased CRP, or leukocytosis.

CASE B. 66-years-old woman, without relevant medical history, who presented fever and myalgias for four days. After this, she also presented skin lesions with dysesthesia. Later, she also presented severe headache. The neurological examination was normal, except for stiff neck. The CT was normal, and the lumbar puncture showed leucorrhachia (mononuclear prevalence).
In both cases, PCR test of the cerebrospinal fluid for VZV was positive, and after a few days with acyclovir treatment the symptoms disappeared.

**Conclusions:** We can appreciate how VZV meningo-encephalitis can vary in its clinical presentation. It is important to have a high degree of suspicion to avoid subsequent complications due to delays in the administration of treatment.
ASSESSMENT OF DIAGNOSTIC APPROACH AND MANAGEMENT OF SUSPECTED ENCEPHALITIC PATIENTS AT OMDURMAN TEACHING HOSPITAL

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Background and Aims:: The objectives of this study were to assess the approach and management of suspected encephalitis cases in Omdurman Teaching Hospital.

Methods:: This study was a descriptive cross-sectional study over 6 months (May to October 2019). The study included 84 patients with suspected encephalitis, selected by convenience sampling. A standardised questionnaire was used to interview patients and the collected data was analysed by SPSS version 27.0.

Results:: The most common presenting symptoms among the study participants were fever and headache (100%), seizures (36.9%) and agitation (28.6%). Neurological examinations showed hemiparesis in 13.1% of patients. Complete blood counts showed lymphocyte predominance in all patients. 65.5% of patients made a full recovery, whereas 26.2% of cases culminated in motor deficit.

Conclusions:: The patients’ outcome was poor as below two-thirds of suspected encephalitis cases recovered fully. The NICE criteria for diagnosis had not been adequately followed, as only a minority of patients had undergone CSF and MRI investigations. Recommendations: Greater adherence to NICE diagnostic criteria must be observed. Documentation of specific reasons is also necessary if neurological imaging is not used. The exact etiology must be identified and targeted antimicrobial treatment must be initiated. If CSF results cannot be obtained in cases of suspected encephalitis, rapid administration of intravenous acyclovir should be included as part of empirical antimicrobial therapy.
ACUTE MEMORY AFFECTION DUE TO VIRAL ENCEPHALITIS WITH HYPOCELLULAR CEREBROSPINAL FLUID (CSF) IN SPITE OF MRI FINDINGS: A CASE REPORT

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Background and Aims:: Herpes simplex virus encephalitis (HSVE) is one of the most potentially fatal infectious central nervous system (CNS) disorders. Thus, early detection is very critical in determining the fate of the case. Clinical history and examination, brain computed tomography, dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI), and lumbar puncture have been used to establish a diagnosis.

Methods:: This case report showed a case of HSVE with hypocellular cerebrospinal fluid (CSF) and rare presentation of memory affection. However, typical MRI findings consistent with HSVE and CSF polymerase chain reaction (PCR) positive for HSV1 DNA, which responded to treatment.

Results:: CT brain showed a normal brain with no mass, lesions, or vascular event. Lumbar puncture for CSF sampling results: shows evidence of hypocellular csf (5cells) with pcr +ve test for HSV 1 MRI brain with contrast result showed left mesial temporal, insular areas of abnormal signal with mass effect in the form of obliteration of the temporal horn and effacement of the cortical sulci with corresponding restricted diffusion. However, no abnormal contrast enhancement was observed.
Conclusions:: HSVE is considered a fatal neurological illness, which can be represented by any symptoms and unusual CSF results. Thus, early intervention and start specific antiviral treatment once a case is suspected to prevent complications and improve outcomes.
OPISTHOTONOS WITH PRESERVED CONSCIOUSNESS IN A PATIENT WITH COINFECTION BY MYCOBACTERIUM TUBERCULOSIS AND MYCOBACTERIUM ABSCESSUS

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Background and Aims:: Tubercular meningitis (TBM) represents 1\% infection caused by Mycobacterium tuberculosis (MTB). Opisthotonos has been reported mainly from data from children with hydrocephalous. Consciousness is depressed in patients developing opisthotonos with further deterioration to coma. CNS infections by Mycobacterium abscessus (MABS) complex are rarely reported and carries a high mortality rate (35-70\%).

Methods:: We present a 16-year-male who was diagnosed as TBM based on clinical, radiological, and microbiological evidence, started on antitubercular treatment (ATT), underwent ventriculoperitoneal shunt for increasing hydrocephalous and initially improved in his symptoms for 2-3 weeks. He worsened and presented with opisthotonos, however the consciousness was preserved.

Results:: CSF examination revealed positive Genexpert for MTB resistant to rifampicin, culture showed MABS. Gadolinium enhanced magnetic resonance imaging showed increasing hydrocephalous, gross cerebral edema with obliteration of cisterns and exudates.

Conclusions:: Opisthotonos in adults with TBM who is already on ATT is an ominous sign. Nontuberculous mycobacteria are ubiquitous with the potential to cause pathological presentations which are indistinguishable from MTB. They are very reported for neurological manifestations and difficult to culture in CSF which is responsible for delay in diagnosis and treatment apart from multidrug resistant MTB.
MALARIA AMONG ADULT SUDANESE COVID PATIENTS BETWEEN THE 4TH OF APRIL 2020 TO THE 15TH OF JANUARY 2021

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Background and Aims:: Malaria can occur on the top of covid19. Aims: To assess the possible link between malaria and covid 19.

Methods:: This is a retrospective cohort study conducted among adult Sudanese COVID-19 patients between the 4th of April 2020 to the 15th of January 2021. 87 of the patients were included.

Results:: Among the 87 patients 64.9 % were males while 35.6 were females. 27.6 % had a positive blood film. 64.7% of the malaria patients had p.falciprum while 35.3% had p.vivax. 52.9% of the patients showed positive RT-PCR for covid 19 with 52.9 % showed positive CT findings. Generalized fatigability was observed in 52.9 % of the patients with malaria followed by headache, nausea, fever with chills, fever with shivering, vomiting and diarrhea in 42.5%,36.8%,20.7%,12.6%,9.2%,9.2% respectively. In covid 19 patients 85.1% had fever and generalized fatigability, Followed by cough, headache, SOB, Sore throat ,myalgia, chest pain, and diarrhea In 73.6 %,59.8, 52.9, 20.7 ,20.7,10.3,5.7 respectively. 13.79 % had malarial pneumonitis, followed by pulmonary edema , choleric malaria, thrombocytopenia and malaria induced hepatitis in 10.39 %,9.2 %, 9.19 %, 6.9% respectively. 8.4% had cerebral malaria while 1.1% had cerebellar syndromes. 44.8 % had ARDS, 17.2% had heart failure, 8% had pulmonary embolism, 8% had stroke, 3.9% had encephalitis and 1.1% had convulsions.

Conclusions:: Malaria and covid 19 have a possible link that they both share similar presentations and complications.
CEREBELLAR HYPERMETABOLISM AND CORTICAL HYPOMETABOLISM IN OPSOCLONUS-MYOCCLUS SYNDROME: TWO CASE REPORTS

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Background and Aims: Opsoclonus-myoclonus syndrome (OMS) is a rare syndrome characterized by opsoclonus, myoclonus, ataxia, behavioral and sleep disturbance. We describe two cases of OMS due to parainfectious condition and with similar brain functional imaging findings.

Methods: Both patients performed brain FGD-PET/MRI at the onset and after 3 months from clinical recovery.

Results: Case one: 54-year-old man presented with one-month history of jerky limbs movements, gait unsteadiness, blurred vision, delusional thoughts. Neurological examination revealed opsoclonus and generalized myoclonus. Blood tests revealed decreased CD4+ and positive HIV viral load. Onconeural anti-neuronal antibodies were negative. CSF showed increased protein level, 14 lymphocytes, oligoclonal bands and HIV viral load higher than on blood. The patient was started on antiviral, high dose steroid and Ig. Brain FDG-PET/MRI before and after three months of treatment showed high cerebellar metabolism associated with widespread cortical hypometabolism reverted in the follow-up scan. Case two: 46-year-old woman with one-week history of fever was admitted for gait unsteadiness and limbs tremor. Neurological examination revealed opsoclonus, cerebellar ataxia and intentional and postural tremor with overlapping myoclonus. Anti-CMV IgM antibodies were positive on blood. CSF examination showed 100 lymphocytes, increased proteins with blood-brain barrier dysfunction. Brain FDG-PET/MRI revealed increased metabolism of cerebellar nuclei and cortex and occipital hypometabolism. The patient was treated with high dose steroids and Ig, with complete recovery. Control brain FDG-PET/MRI after three months was normal.

Conclusions: These results may suggest that cerebellar over-activation is involved in developing OMS. Increased cerebellar metabolism and posterior cortical hypometabolism may be the functional correlates of OMS due to parainfectious encephalitis.
EPILEPTIC PARTIALIS CONTINUA (EPC) AS CAN BE AN INITIAL PRESENTATION OF HIV - A RARE CASE SCENARIO

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Background and Aims:: BACKGROUND EPC as initial presentation of HIV is very rare AIM To disseminate that EPC could be initial presentation of HIV

Methods:: 21 yr male presented with witnessed seizure(seminology characterized by jerky movements of left angle of mouth and left upper limb with up rolling eyeball and tongue bite followed by postictal confusion). Managed conservatively by antiepileptic, a day later he developed repetitive involuntary clonic-myoclonic movement of left arm with facial deviation to right ,no loss of consciousness. He was then managed by sequential antiepileptics showing no significant reduction in seizure. EXAMINATION Hypotonic and scanning dysarthria, EPCs present in Left upper (UL) & lower limbs(LL) ,Power – UL (Rt & Lt) - 4/5 & LL (Rt & Lt) - 3/5, DTR – Lt Biceps and knee 3+ others 2+, B/L Plantar Extensor response , Dysmetria,titubations note HIV 1 positive(ELISA ) confirmed by Western Blot ,HIV RNA – 163771 IU/L ,CD4 – 95 cells/c.mm, HIV 2 - negative, CSF Sugar - 82 mg% ,Protein : 40.8gm%,Gram / ZN/ Fungal/JC Virus- Negative , RBC -03 & WBC -02cells/c.mm, no malignant cells , ADA – 1.0 IU/L , ANA,Auto Immune Encephalitis panel - negative He was diagnosed as a case of HIV Encephalopathy – EPC ,Managed with TLE regime (ART) and appropriate prophylaxis for opportunistic infections .EPC controlled with 04 anti epileptics (Oxcarbazepine,Levitracetam,Lacosamide and Perampanel). He responded well.

Results::
Conclusions:: EPC in HIV infected person is rare and same could be a rarest initial presentation. Anti-epileptics – ART interactions needs to be kept in mind.
INVASIVE RHINO-ORBITO-CEREBRAL ASPERGILLOSIS PRESENTING AS MULTIPLE CRANIAL NEUROPATHIES – A CASE REPORT

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Background and Aims:: Presenting as a complication of paranasal fungal sinusitis, due to continuous spread of an invasive agent to adjacent tissues, the rhino-orbito-cerebral syndrome is frequently associated with Aspergillus or Mucor infections.

Methods:: A case of a 66-year-old patient with rapidly progressive cranial neuropathies in the context of an invasive Aspergillosis is presented.

Results:: A 66-year-old male patient, with a myelodysplastic syndrome and history of recent severe COVID19 infection, was admitted to the Emergency Department due to periorbital pain and fever. On physical examination, the patient displayed III, IV and VI left cranial neuropathies, decreased visual acuity and left hearing loss. A septic thrombosis of the cavernous sinuses was initially admitted and antibiotic therapy started. However, on the following day, peripheral facial diplegia, V2 paresthesia and dysarthria were identified. An MRI was conducted, revealing bilateral ethmoiditis and post-septal left orbital cellulitis, and PAS staining of a nasal biopsy identified spores and hyphae. After admission to an Infectious Diseases unit, the patient clinically deteriorated, with pre- and post-septal cellulitis and progression of periorbital edema to the contralateral eye. A positive PCR test for Aspergillus spp was detected in the CSF and nasal mucosa. Thirty-one days later, after antifungal therapy (anfotericin B, isavuconazole), clinical improvement was registered.

Conclusions:: Patients with severe COVID-19, subjected to corticosteroids, are particularly prone to develop fungal infections due to immune system dysfunction. This clinical case highlights the relevance of fungal etiology in the differential diagnosis of ophthalmoplegia in immunosuppressed patients, whose early diagnosis and treatment is essential, excluding potentially fatal infections.
WHEN HERPES LINGERS ON: A RARE COMPLICATION OF ACUTE HERPES SIMPLEX
ENCEPHALITIS

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Background and Aims:: Herpes simplex encephalitis (HSE) is the most common viral encephalitis.
Rarely chronic granulomatous inflammation in response to persisting herpes virus antigens in the brain
may occur. We aim to describe the clinical course of a patient with chronic granulomatous HSE (CGHSE)
which was proven by brain biopsy.

Methods:: Clinical course and serial brain MRIs were reviewed. Biopsy of the right temporal lobe was
performed.

Results:: A 16-year-old boy presented with acute febrile encephalopathy. Brain MRI showed T2
hyperintensities in the right medial temporal lobe. He was treated on lines of HSE and he recovered with
acyclovir. He had recurrent seizures and mild cognitive decline 1.5 months after the acute illness. Serial
MRIs at 2, 6, and 8 months post-HSE showed progressive increase in signal changes involving the entire
right temporal lobe and left mesial temporal region with gyriform enhancement. Work up for immune-
mediated causes (autoimmune encephalitis, sarcoid and vasculitis) were negative. CSF PCR for HSV
was negative but antibody titers were elevated. Brain biopsy revealed granulomatous angiitis.
Immunohistochemistry for HSV antigen was negative, but PCR on the brain tissue was positive for HSV
DNA. The patient was diagnosed to have CGHSE and treated with valacyclovir. There was good clinical
and radiological response at 24 months follow up.

Conclusions:: CGHSE occurs in a small number of patients post-acute HSE. Diagnosis may be aided by
brain biopsy that demonstrates granulomatous inflammation with evidence of persistent HSV
antigens/DNA. This peculiar entity is treatable and has a reasonably good outcome.
BILATERAL OPTIC TRACT ENHANCEMENT: AN UNUSUAL IMAGING FINDING IN NEUROSYPHILIS

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Background and Aims:: The differential diagnosis of lesions affecting the optic tract commonly include infectious, inflammatory, and neoplastic conditions. We aim to describe a rare but treatable cause of optic tract enhancement.

Methods:: Brain MRI, visual evoked potentials (VEP) and cerebrospinal fluid analysis (CSF) were carried out.

Results:: A 44-year-old gentleman presented with 2 months history of intermittent blurred vision, transient headaches and unsteadiness while walking. Six months prior to onset of these symptoms; he had hematuria which was treated with oral antibiotics. After 8 weeks he developed a diffuse maculopapular rash over the trunk and involving the palms and soles. General physical and neurological examination was normal. Visual acuity, perimetry and VEP were normal. MRI revealed slight enlargement of the right optic tract with central T2 hypointensity and enhancement within the both optic tracts (right>left). In addition, subtle leptomeningeal enhancement was seen in the upper cervical cord. CSF analysis revealed lymphocytic pleocytosis (42 lymphocytes/mm³) with elevated protein (66.2 mg/dL). CSF and serum Venereal Disease Research Laboratory (VDRL) and Treponema pallidum hemagglutination test (TPHA) were positive (1:2560). Patient was treated with Penicillin and had clinical and serological improvement at 3-months follow up.

Conclusions:: Syphilis affects the nervous system in 5-30% of infected individuals. The manifestations are varied and temporally related to the time of acquisition of the infection. Perivascular lymphocyte aggregation results in ‘gumma’ formation. Neurosyphilis should be considered as a differential diagnosis in patients with enhancing lesions in the optic tract in the setting of CSF pleocytosis.
INTRATHECAL HYALURONIDASE FOR IMPENDING AND SYMPTOMATIC ARACHNOIDITIS IN TUBERCULAR MENINGITIS.

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Background and Aims:: CNS Tuberculosis, the most rampant infection of the developing world, clinicopathologically can occur alone or combined as Tubercular Meningitis, Tuberculomas (intracranial and/or spinal), Arachnoiditis (basal, optocochiasmatic, spinal) or Myelitis. The viscous exudates in basal cisterns cause Optocochiasmatic arachnoiditis[1], and nodular, thickened, clumped nerve roots called Lumbosacral arachnoiditis.[2] We herein propose use of intrathecal hyaluronidase, as adjuvant for symptomatic as well as impending arachnoiditis.

Methods:: •A prospective cohort study including 48 patients of TB Meningitis (15-65 yrs) with 4 treatment groups (Group A-D) was designed. •Group A (n=11) and B (n=14) had patients of Symptomatic Arachnoiditis (SA) defined as those with new diminished visual acuity & prolonged P100 latency (Visual Evoked Potential), deranged Barthel index and/or hydrocephalus in neuroimaging (without obstructive tuberculomas). •Group C(n=10) and Group D(n=13) were Impending Arachnoiditis (IA)- Those having CSF Protein >250mg/dl[1] and/or MRI evidence of arachnoiditis without yet manifested symptoms. Standard treatment (ATT + Steroids) for Group A & C, adjuvant Intrathecal Hylase (1500 IU biweekly for first 2 weeks, thereafter weekly for 4 weeks) for Group B & D.
Patients having residual/worsening deficits at completion of intensive phase at 2 months - 54.5% (6) from Group A, 21.4% (3) from Group B, 50% (5) patients from Group C and 15.3% (2) from Group D.

Only 1 patient had skin reaction on sensitivity testing, was excluded from study.

Conclusions:
1. Optochiasmatic & Spinal arachnoiditis was common in TBM patients with initial CSF protein >250mg/dl.
2. Incorporating early administration of intrathecal hyaluronidase in TBM treatment protocol can benefit impending as well as symptomatic arachnoiditis (p value < 0.01).
ATYPICAL SPINAL TUBERCULOSIS WITH ISOLATED SOLITARY VERTEBRAL BODY INVOLVEMENT

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Background and Aims:: Typical spinal tuberculosis affects the continuous vertebral levels and causes narrowing of the adjacent disc space and bone destruction. However, atypical form of spinal tuberculosis is difficult to distinguish from malignancy, leading to misdiagnosis and inadequate treatment.

Methods:: A 40 year old male patient, farmer by occupation and having no prior comorbidities, was admitted with gradually progressive low back pain for 3 months and weakness of both lower limbs since 2 months.

Results:: On examination, there was wasting and hypotonia in both lower limbs and grade 1 power in both lower limbs, absent knee and ankle reflexes, mute plantars and spinal tenderness at lumbosacral region at L2-L3, with no gibbus deformity. X-ray lumbosacral spine showed anterior vertebral scalloping of L2 with sparing of the disc. MRI spine revealed altered signal intensity lesion in L2 vertebral body which was hypointense on T1W, hyperintense on T2W and STIR images, with normal appearing adjacent intervertebral disc along with large right paravertebral and epidural soft tissue component resulting in compression of traversing nerve roots at same level. Histopathology of L2 vertebral body revealed epithelioid cell granulomas suggestive of TB spine.
Conclusions: Spinal tuberculosis involving only one vertebral body without disc involvement is a rare presentation. Imaging studies are an important tool for characterizing the lesion, performing biopsy, evaluating the success of treatment and detecting any complications in the follow-up.
PROGRESSION IN COGNITIVELY IMPAIRED PATIENTS WITH ATRIAL FIBRILLATION: AN OBSERVATIONAL STUDY

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Background and Aims:: Data about progression in patient with AF and concomitant cognitive impairment are not known. Moreover, there is no agreement in the scientific literature about anticoagulants use in these patients.

Methods:: We analyzed cognitive impairment progression in n=90 outpatients with any grade of cognitive deficit regularly seen from January 2015 to February 2021. Forty-five patients (50%) were affected by AF (AF+). AF+ and AF- patients were matched 1:1 for sex, age, years of education and MMSE at presentation. Mean MMSE (± SD) at entry study was 23.6 ± 3.8 and 23.4 ± 3.9 for AF+ and AF- patients, respectively. Mean follow up was 22 months and was not significantly different between the two groups. Cognitive decline was inferred using Mini-Mental State Examination (MMSE) score collected in subsequent visits, calculating a Disease Progression Index (DPI) as raw MMSE decline over time.

Results:: DPI in AF+ was 3 times faster than in AF- patients (-0.18 ± 0.25 vs. -0.06 ± 0.24, AF+ vs. AF-, respectively) (figure 1). Among the FA+ patients, those using anticoagulants (AC+) did not show any significant between-group difference in cognitive decline compared to those not using them (AC-); however, the sample size of this latter group was small (figure 2).
Conclusions:: Our results confirm the worse outcome in global cognitive function for cognitively impaired AF+ subjects compared to those without AF. Albeit preliminary, our results also suggest that the use of anticoagulants seems not to significantly affect cognitive decline; an increase in sample size is necessary to confirm this latter result.
Background and Aims:: Nursing homes for people with Dementia are a fundamental resource for disease management; non pharmacological approaches are used in these structures. An emerging reality in this field is “museum-therapy” (MT), an experience born at the Museum of Modern Art of New York City and recently arrived in Italy. In this study we investigated the efficacy of MT in a group of patients with dementia.

Methods:: 30 patients affected by various typologies of Dementia underwent a standard rehabilitation program in our Institute (~ 80 days). Patients were randomized in two groups: one group of 15 patients participated to three structured visits at the National Gallery of Modern Art of Rome; the other group in the same time was occupied by other open air extra activities. One week before and one week and one month after the end of the visits patients were double-blind evaluated with an extensive neuropsychological battery. ANOVA and Student's t paired groups were conducted to analyze data.

Results:: The two groups of patients did not differ for clinical/socio-demographical variables. As expected both the group of patients improved their performances in tests of memory, attention and executive functions and reduced behavioural disturbances (p<0.01). Patients who partecipated to MT significantly improved their performances in the tests of cognitive estimation and pragmatic abilities (p<0.001), this did not happen for the other group.

Conclusions:: MT demonstrated to have positive effects on cognition of demented patients, different from those ones usually involved by other more conventional techniques. MT could become a precious resource for dementia’s management.
OLIVE POLYPHENOLS AND BIOAVAILABLE GLUTATHIONE: PROMISING RESULTS IN PATIENTS DIAGNOSED WITH MILD ALZHEIMER’S DISEASE

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Background and Aims:: Recent studies highlighted a potential efficacy of olive polyphenols and of a derivatized form of glutathione to counteract neuropathology affecting specific brain regions at early AD stages. We performed a cross-over clinical trial to evaluate their potential benefits in mild AD.

Methods:: 40 patients diagnosed with mild AD according to IWG-2 criteria were enrolled in a twelve month trial and randomly assigned to two groups of equal sizes: Group 1, receiving treatment in the first six months and no treatment for the second six months, and Group 2, receiving no treatment for the first six months, and treatment for the second six months. Treatment consisted in a nutraceutical formulation comprising 50 mg/cps S-acetyl glutathione and 80 mg/cps oleuropein administered bid. Patients should have undergone a complete set of neuropsychological tests at the moment of the enrollment (T0), after six months (T1) and after twelve months (T2). Due to the difficulties related to COVID-19 emergency, only 10 patients in Group 1 and 8 in Group 2 could be enrolled. They could be evaluated only at T0 and T1.

Results:: All cognitive functions resulted stabilized or improved following the treatment, while behavioural disturbances significantly diminished.

Conclusions:: If further research will confirm these data the described treatment could be proficiently adopted for patients with mild AD as well as a preventive tool for those at risk of developing dementia.

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MRI AND COGNITIVE TESTS-BASED SCREENING TOOL FOR DEMENTIA

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Background and Aims:: Establishing an association between cognitive status and either disease- or age-related neuronal loss reflected by MRI may have a diagnostic value. Deep Learning (DL) is an AI technique that allows for the discovery of such an association by building models that can predict cognitive performance from the brain structure. The relationship between the brain structure and its functioning may have patterns specific for preserved versus impaired cognition. The models trained on healthy populations will not predict cognitive status accurately in cognitively impaired individuals. We aimed to work out a screening tool for MCI and dementia.

Methods:: We tested if a gap between the actual cognitive performance and the one predicted from MRI is informative as a marker of cognitive deterioration. To calculate the gap we designed a DL regression model and trained it on T1W MRI images of 422 normal controls (NC). An outcome of a model was the result of a cognitive assessment with MMSE, ADAS-cog, RAVLT, DSST, and TMT tests. This allowed us to build five models and compare their performance in NC with 377 patients with Alzheimer’s disease (AD).

Results:: In AD cognitive gap values differed significantly from NC. For MMSE they were 6.23±3.08 in AD versus 1.09±0.73 in NC; p<0.0001. The distinction of AD and NC had 0.9951 sensitivity, 0.9919 specificity, and 0.9935 accuracy.

Conclusions:: The application of DL to a combination of MRI and cognitive assessment may provide computer-aided diagnostics of AD.
EFFECTS OF BUTYLPHTHALIDE ON COGNITIVE FUNCTION AND INFLAMMATORY STATUS IN PATIENTS WITH ACUTE CEREBRAL INFARCTION COMPLICATED WITH COGNITIVE DYSFUNCTION

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Background and Aims:: Acute cerebral infarction not only leads to physical functional impairment, but also leads to non-physical dysfunction. Butylphthalide can reduce the poor prognosis of non-physical dysfunction after acute cerebral infarction, and effectively improve the cognitive function of patients. Aims: To investigate the effects of butylphthalide on cognitive function and inflammatory status in patients with acute cerebral infarction complicated with cognitive dysfunction.

Methods:: 100 patients with acute cerebral infarction complicated with cognitive dysfunction were divided into observation group and control group. Control group was treated with aspirin and atorvastatin. Observation group was additively treated with butylphthalide for 3 months. Compared two groups with simple mental state check table (MMSE), Montreal cognitive assessment scale (MOCA), serum High sensitivity C-Reactive Protein (hs-CRP), pentraxin3(PTX-3), interleukin-6 (IL-6) levels, the incidence of the poststroke dementia (PSD) and adverse reactions.

Results:: After treatment, MMSE and MOCA scores in observation group were more higher than control group compared with them in before, while serum hs-CRP, PTX-3 and IL-6 levels were more lower than those in control group (P<0.05). The incidence of PSD and the adverse reactions in the observation group were lower than those in the control group, but the differences were not statistically significant (P>0.05).

Conclusions:: Butylphthalide in the treatment of patients with acute cerebral infarction complicated with cognitive dysfunction can effectively improve their cognitive function, inhibit inflammatory response.
KNOWLEDGE OF ALZHEIMER’S DISEASE AMONG MEDICAL STUDENTS AND HEALTHCARE PROVIDERS IN SUDAN

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\textbf{Background and Aims::} The objective of this study was to assess knowledge of Alzheimer's disease among medical students and healthcare providers in Sudan.

\textbf{Methods::} In this cross-sectional study, that was conducted in Sudan during the period from July to December 2020, we used Google forms to collect data from 217 medical students and healthcare providers using Alzheimer’s Disease Knowledge Scale (ADKS). ADKS is a widely used validated instrument that measures what people know about Alzheimer disease using 30-item true/false questionnaire across seven critical knowledge domains: risk factors, symptoms, assessment and diagnosis, disease trajectory, life impact, treatment and management, and caregiving.

\textbf{Results::} Our studied population consisted of doctors (n = 108), medical students (n=25), dentists and pharmacists (n=40) and other healthcare providers (n=44). 77.4 % were females. The mean age was 29 years (SD = 6.5), and When rating their knowledge from 0-10, Our participants' mean value was 5.3 ± 2.1. Regarding ADKS the mean knowledge score (out of 30) is 20.6 ± 2.8. The best average score was treatment and management 86.8%, followed by life impact 78.3%, assessment and diagnosis 72.4%, disease trajectory 71.5%, symptoms 62.7%, caregiving 59.2%, and risk factors 59%. We did not detect any significant association between the average overall score and gender, occupation, source of information, or having a relative with Alzheimer’s disease.

\textbf{Conclusions::} Specific knowledge deficits were observed in domains focusing on risk factors, symptoms and caregiving for Alzheimer’s disease.
POST-STROKE COGNITIVE IMPAIRMENT AND THE BALANCE OF COAGULATION AND FIBRINOLYSIS

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Background and Aims:: Post-stroke cognitive impairment (PCI) contributes greatly to the global stroke burden. In recent years, the role of hemostasis in PCI is acknowledged more and more. This study aimed to evaluate the connection between PCI and coagulation/fibrinolysis balance.

Methods:: Thirty-two ischemic stroke patients with no aphasia were included in the study. At admission, the NIHSS scores were recorded, and blood plasma samples were obtained. Using a Thrombodynamics analyzer, two tests were done to assess the coagulation/fibrinolysis balance. The first test was performed according to the standard Thrombodynamics protocol; the second test was performed with the addition of a recombinant tissue plasminogen activator (rTPA). Using Karmin software, hemostasis potential (HP) and fibrinolysis potential (FP) were calculated. PCI was assessed using Montreal Cognitive Assessment (MoCA) scale 10 to 14 days after admission. Local ethical committee approved the study.

Results:: In univariate and multivariate analyses that included age and NIHSS at admission as covariates, hypercoagulation and higher HP at admission were found to be associated with lower MoCA scores (by -1.062 in univariate model [95% CI from -1.884 to -0.240, p=0.013] and -0.872 in multivariate model [95% CI from -1.592 to -0.152, p=0.019] for every ten points of HP). Moreover, better response to rTPA and higher FP were associated with higher MoCA scores (by 1.206 in univariate model [95% CI from 0.183 to 2.228, p=0.022] and 1.017 in multivariate model [95% CI from 0.138 to 1.895, p=0.025] for every ten points of FP).

Conclusions:: Hypercoagulation/hypofibrinolysis are associated with lower early MoCA performance and PCI in ischemic stroke.
THE CORRELATION BETWEEN SERUM CRP, NSE, CCL2 AND COGNITIVE IMPAIRMENT AFTER ACUTE ISCHEMIC STROKE

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Background and Aims:: Early detection of cognitive dysfunction after stroke, and early intervention to reduce the patient and family great mental and economic burden is particularly important. Aims: To explore that Neuron Specific Enolase (NSE), C-Reactive Protein (CRP) and Chemokine CC motif 2 (CCL2) can become the screening and early warning organism of cognitive dysfunction after acute ischemic stroke, which is convenient, quick and does not significantly increase the cost of diagnosis and treatment the possibility of scientific indicators.

Methods:: 200 patients with acute ischemic stroke and 100 healthy people were selected, and divided into normal cognitive function group (93 cases), cognitive dysfunction group (107 cases) and control group (100 cases). To study the relationship between serum NSE, CRP and CCL2.

Results:: 1. The serum concentrations of NSE, CRP and CCL2 in patients with acute ischemic stroke were higher than those in normal control group (P<0.05). 2. The levels of NSE, CRP and CCL2 in patients with cognitive impairment after acute ischemic stroke were higher than those in patients without cognitive impairment after stroke (P<0.05). 3. The cognitive scores were positively correlated with serum NSE, CRP and CCL2 (r=0.21, P<0.05).

Conclusions:: The serum NSE, CRP and CCL2 can be used as biological detection indicators of cognitive dysfunction after acute ischemic stroke. It can be used as an effective index for clinical diagnosis, disease condition and prognosis evaluation of cognitive dysfunction after acute ischemic stroke.
THE BEHAVIORAL VARIANT OF FRONTOTEMPORAL DEMENTIA: LINKING CEREBELLAR MRI ALTERATIONS TO BEHAVIORAL AND AFFECTIVE SYMPTOMS

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Background and Aims:: Frontotemporal dementias (FTDs) are progressive neurodegenerative disorders associated with grey matter (GM) loss in frontal and temporal brain regions (Rascovksy et al., 2011) and presenting with marked behavioral symptoms and/or language deficits. The Behavioral variant of FTD (bvFTD) is clinically characterized by insidious changes in personality, interpersonal conduct and emotion processing (Piguet, et al 2017). Considering its role in higher-level functions (Schmahmann & Sherman, 1998) the cerebellum was recently proposed to be implicated in FTD pathophysiology (Yu Chen et al., 2019) although its specific contribution to bvFTD symptoms still needs to be clarified. Aim of the present study was to assess cerebellar GM changes in patients with bvFTD and their potential association with affective symptoms.

Methods:: Patients with bvFTD and healthy subjects (HS) underwent MRI scanning at 3.0T with acquisition of T1-weighted volumes. Voxel-based morphometry (VBM) was performed to compare cerebellar GM volumes between patients and HS. Patients' behavioral measures were also acquired to be correlated with MRI data.

Results:: Compared to HS, bvFTD patients showed regional GM loss in the right Crus I, the left lobule VI, the left Crus I and Crus II of the cerebellum.

Conclusions:: These findings indicate a specific pattern of cerebellar GM atrophy that involves regions primarily connected to the prefrontal cortex (Kelly & Strick, 2003). We argue that an association exists between cerebellar GM changes and damage to corresponding prefrontal regions mediated by cerebro-cerebellar loops which may account for the behavioral and affective symptoms observed in bvFTD.
Background and Aims: Subjective Cognitive Decline (SCD), defined as a subjective decline in cognitive function without an objective impairment on tests, has been demonstrated to be an at-risk stage for dementia, which already costs around a trillion dollars per year. This research aimed to ascertain what has been published around the world on that subject.

Methods: Authors searched MEDLINE, EMBASE, PubMed, among others for complete articles from 2014 to 2020, in English and Spanish, using the keyword “Subjective Cognitive Decline” and “Deterioro Cognitivo Subjetivo”

Results: Of 3470 results, 487 were eligible articles. The largest publishers were the USA, China, Netherlands, and Germany, each with approximately 10% or more of the total publications. In 2014 8 articles were published, contrasting with 167 in 2020 (an increase of almost 2000%) with 87% of the total published in high-income countries. Unexpectedly in the USA, 24% of the articles used biomarkers, contrasting with China, with 68%. The mechanisms of SCD was the most studied subject (33,14%), followed by Clinical manifestations (20,98%) and prognostics (14,51%), and there were 3 articles relating the condition to COVID-19.

Conclusions: This review demonstrates an increasing number of publications and relevance of the topic, with a concentration of articles in some countries, especially in high-income. Among middle-income countries, China stands out with a growing number of publications. The main interest of the articles were the mechanisms, especially biomarkers, the presentation, and the relation of the condition with dementias. The association to COVID-19 studies demonstrates new concerns regarding the topic of cognition and highlights its importance.
Background and Aims:: Mild Cognitive Impairment (MCI) is a dynamic state which has evolved into a highly defined condition due to its association with dementia syndromes. There are no published data on the demographic and clinical characteristics of MCI in the Philippines. These data will help in defining the population at risk for the condition and in modifying the factors for its prevention.

Methods:: From 2010 to 2019, 446 subjects were diagnosed with MCI based on the criteria published by the International Working Group on MCI. The demographic profile, vascular risk factors, and Vitamin B12, Vitamin D, and homocysteine levels were reviewed. Results of neuropsychological tests, such as Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), Mini-Mental State Exam (MMSE), and locally-adapted Montreal Cognitive Assessment-Philippines (MoCA-P), were collected. Neuroradiologists reviewed the MRIs to determine the Fazekas score.

Results:: The median age was 72 years [34 – 99] with 58.3% females. The median years of education was 14 [4 – 28]. Median ADAS-Cog, MMSE, and MoCA-P scores were 11.3 [0 – 37.7], 27 [13 – 30], and 21 [4 – 30], respectively. Hypertension and dyslipidemia were present in 67.0% and 38.3%, respectively. Normal homocysteine, Vitamin B12, and Vitamin D levels were found in 62.8%, 60.2%, and 48.2%, respectively. The median Fazekas was 1 (58.8%).

Conclusions:: This is the first study to document the demographic and clinical profile of Filipinos with MCI in a clinical setting. This review serves as a foundation for increased understanding of MCI with the long-term goal of controlling the factors which may impact its prevention.
NEUROLOGICAL SOFT SIGNS IN NEURODEGENERATIVE DEMENTIAS: A PILOT STUDY

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Background and Aims:: Neurological Soft Signs (NSS) are sensory-motor abnormalities linked with cerebellar and microstructural subcortical white matter alterations, which are not systematically evaluated during standard neurological examination. Although historically observed in psychiatric conditions, NSS have been recently associated with migraine, mild cognitive impairment and Alzheimer’s disease (AD), and correlated with age and apoE polymorphisms. However, no study to date has evaluated the burden of NSS in other types of dementia. Our research aims to confirm the increase of NSS in AD patients, and extend their assessment to fronto-temporal dementia (FTD), cortico-basal syndrome (CBS) and Lewy-body dementia (LBD), correlating them with the severity of cognitive impairment.

Methods:: Mini-Mental State Examination (MMSE), Frontal Assessment Battery (FAB) and a modified version of the Heidelberg NSS Scale have been administered to 75 patients with mild and moderate dementias and 30 healthy matched controls.

Results:: Demented patients showed almost 3-times higher NSS values compared to controls (p<0.05), with CBS/LBD patients bearing the highest burden, followed by AD and FTD patients, with significant between-groups differences (p=0.003). Statistically significant differences in single NSS scale items across different types of dementia were observed. NSS inversely correlated with MMSE and FAB, and positively correlated with disease duration only in AD subjects.

Conclusions:: Our work suggests that NSS are significantly more expressed in neurodegenerative dementias compared to healthy controls, especially in subcortical types. The modified version of the Heidelberg NSS Scale could represent a helpful instrument in the differential diagnosis of cognitive decline, with a potential role in the follow-up.
Background and Aims:: It is well known that persons with Alzheimer’s disease often present with word finding difficulties since the early phases of the disease. Although speech therapy might be indicated for treating this disorder costs, mobility and recently pandemic issues often hinder access to the cure. Here we provide experimental evidence supporting the feasibility and efficacy of a telemedicine approach based on word repetition for treating anomia in AD.

Methods:: Inclusion criteria were diagnosis of AD, pathological picture naming performance and spared word repetition. The treatment protocol lasted 1 month and was entirely administered at the distance by means of a tablet. The protocol comprised the following phases: item selection (3 words sets with equal subjective difficulty were selected, as control and experimental sets); baseline (the words set were named 3 times each to define a baseline level); training (the two experimental sets were assigned each to a training condition. Both conditions consisted in repeating the target word coupled with the corresponding picture but the presentation order of the picture and the to-be-repeated word varied across condition. outcome (the 3 word sets were named 3 times after training). A Logistic mixed model was carried over to analyse the effect of training on the control and experimental sets.

Results:: Naming significantly improved on the trained words with only minor hints of generalisation to the untreated items.

Conclusions:: Our results confirmed the feasibility and efficacy of telemedicine to improve access to speech therapy in AD.
CONNECTED SPEECH DEFICIT AS AN EARLY HALLMARK OF CSF-DEFINED ALZHEIMER'S DISEASE AND CORRELATION WITH CEREBRAL HYPOPERFUSION PATTERN

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Background and Aims:: There is still a growing interest for the detection of early and non-invasive biomarkers for diagnosis of prodromal Alzheimer's disease (AD). Although progressive episodic memory impairment is the typical predominant feature of AD, communicative difficulties can be already present at the early stages of the disease and could represent an early non-invasive AD biomarker. This study investigate narrative discourse production deficit as a hallmark of cerebrospinal fluid (CSF) defined prodromal AD and its correlation with cerebral hypoperfusion pattern.

Methods:: Narrative assessment with a multilevel procedure for discourse analysis was conducted on 28 subjects with Mild Cognitive impairment (15 MCI due to AD; 13 non-AD MCI) and 28 healthy controls. Diagnostic workup included CSF AD biomarkers. Cerebral hypoperfusion pattern was identified by SPECT image processing.

Results:: Discourse analysis of global coherence and lexical informativeness indexes allowed to identify AD-MCI from non-AD-MCI and healthy subjects. These findings could suggest loss of narrative efficacy as a possible early clinical hallmark of Alzheimer's disease. Furthermore, a significant correlation of global coherence and lexical informativeness reduction with SPECT hypoperfusion was found in the dorsal aspect of the anterior part of the left inferior frontal gyrus, supporting the hypothesis that this area plays an important role in communicative efficacy and, in particular, in semantic selection executive control.

Conclusions:: This study contributes to the understanding of the neural networks for language processing and their involvement in prodromal Alzheimer's Disease. It also suggests an easy and sensitive tool for clinical practice that can help identifying individuals with prodromal Alzheimer's Disease.
DEMENTIA IN PAKISTAN: RESULTS FROM OUR REGISTRY AT A TERTIARY CARE PRIVATE UNIVERSITY HOSPITAL

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Background and Aims:: To analyze data of our dementia patients enrolled from 2010 to 2015 from our dementia registry and to report their epidemiology, frequency, investigations and management.

Methods:: All patients with dementia coming for neurology consultation who gave their consent were enrolled in the registry from October, 2010 to June, 2015. The registry was approved by our Institutional Review Board and Ethics Committee. Demographic and clinical data was recorded on a predesigned dementia registry form and included clinical features, pertinent investigations and cognitive assessment: Mini Mental State Examination, Neuro Psychological Inventory, Beck Depression Inventory and Beck Anxiety Inventory. Forms with incomplete data were excluded and data was entered in SPSSv23 for analysis. A total of 267 patients were included for final analysis.

Results:: Out of 267 patients, 55.9% were male. The mean age was 69.3 ± 10.96 years. 26.20% were smokers. 32.96% had Alzheimer’s disease, mixed Alzheimer’s/vascular dementia comprised 23.22%; Parkinson’s disease dementia: 18.35%; Lewy body dementia: 4.87%, Mild Cognitive Impairment: 3.37%, Frontal lobe dementia: 4.12%, Huntington’s disease dementia: 1.49%, Primary progressive aphasia: 1.12%; Creutzfeldt-Jakob disease: 1.50%; others: 5.99%. MRI was done in 36.70% and CT scan in 23.60%. Medications used were Rivastigmine in 15.70%, Donepezil in 6.40%, Galantamine in 5.20% and Memantine in 9.00%.

Conclusions:: Alzheimer’s disease was the most common type of dementia in our patients followed by Mixed Alzheimer’s/vascular dementia and Parkinson’s disease dementia. MRI and CT scan were the main radiological investigations. Only 36.3% opted for symptomatic treatment with cholinesterase inhibitors or memantine.
DONEPEZIL MODULATION OF BETA-AMYLOID Oligomer Phagocytosis IN PERIPHERAL MONOCYTES. BED TO BENCH OBSERVATIONS FROM ALZHEIMER'S DISEASE PATIENTS.

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Background and Aims:: Beta-Amyloid (Abeta) aggregates are reputed to play a central role in AD pathogenesis, partly by triggering neuroinflammation. Peripheral monocytes can shift into the CNS, hence participating in Abeta oligomer clearance. Donepezil's anti-AD mechanism remains largely elusive; however, it can interact with monocyte a7nAChR that is involved in Abeta phagocytosis. We believe that by binding to a7nAChR, Donepezil can modulate Abeta internalization driven by both a7nAChR and TREM2.

Methods:: Differentiated monocytic cell line U937 or differentiated monocytes from AD patients were treated for 24 h with 125 pM Abeta42 oligomers or methyllycaconitine (MLA, a7nAChR inhibitor) and/or pre-treated with Donepezil. Western blot and Real Time-PCR were performed. Phagocytosis was assessed by confocal microscopy analyses with fluorescent Abeta. 20 AD patients (n=10 treated with Donepezil and n=10 naive) and n=10 controls were recruited from our Neurology unit for TREM2 assessment.

Results:: In U937 cells, Abeta was able to significantly reduce TREM2 levels, while co-administration of Donepezil significantly restored them; neatly, this action was blocked by adding MLA. A rise in Abeta internalization after treatment with Donepezil was demonstrated by confocal microscopy studies and this tendency was reverted by MLA. The study in treated and untreated AD patients showed a decrease of TREM2 mRNA levels in AD with respect to controls. Conversely, amongst AD patients, those taking Donepezil presented higher TREM2.

Conclusions:: Our data indicate that on peripheral monocytes Donepezil, by interacting with a7nAChR, might contribute to Abeta clearance, by decreasing neuroinflammation thus favouring TREM2's action.
CARDIOVASCULAR RISK FACTORS AMONG ELDERLY WITH COGNITIVE IMPAIRMENT IN URBAN PRIMARY CARE

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Background and Aims:: Background Cardiovascular (CV) risk factors are common in elderly but their frequency in those with cognitive impairment is not known. Also, the relationship that they have with cognitive impairment is complex and under investigation. It has been stressed that controlling CV risk factors can reduce risk of cognitive decline. Majority of the data in this regard has come from the tertiary care institutions and ours is first such study assessing frequency of vascular risks and their relationship with cognitive impairment in primary care setting. Aim A cross sectional study was conducted to assess the frequency of CV risk factors among elderly in primary care in Western India, screen them using mini-mental state examination (MMSE) and see if there was any relationship of the same with cognitive impairment.

Methods:: Material & Methods A total of 204 elderly (Mean age=66.61±6.63; M:F=131:73) coming to primary care centre were examined using MMSE for cognitive impairment. Written records were examined for the presence of CV risks e.g. diabetes, hypertension/ & diabetes together, stroke and coronary artery disease.

Results:: Results Frequency of CV risk factors in those with cognitive impairment was 84/204 (41.2%) and in those without cognitive impairment was 31/204 (26.9%). A Chi Squared test of proportion showed values to be statistically significantly different (p-value=<0.001. Odds Ratio was calculated to be 6.5 (p-value=<0.0001).

Conclusions:: A higher frequency of common cardiovascular risk factors were observed among those with cognitive impairment compared to those who were cognitively normal elderly.
DIFFERENTIATION OF MILD COGNITIVE IMPAIRMENT (MCI) PROGRESSION TO ALZHEIMER DISEASE (AD) VS DEMENTIA WITH LEWY BODIES (DLB): IS THIS POSSIBLE NEUROPSYCHOLOGICALLY?

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Background and Aims:: Aim of the present review was to describe and compare the neurocognitive features of MCI which could predict its progression to DLB vs AD.

Methods:: A literature review in the Pubmed database has been made, after the year 2005, using the key-words neuropsychological assessment; MCI; AD; DLB. Seventeen relevant articles have been found.

Results:: Data from most studies supports that, in MCI, impairment in executive, attentional and visuospatial functions, as well as letter fluency and fluctuating concentration are mainly related to progression to DLB. In contrast, prominent episodic and recognition memory deficits are mostly found in MCI which progresses in AD. Furthermore, non-amnestic MCI has been related mainly to progression in DLB, whereas the amnestic type to AD, although memory loss may not necessarily predict the development of AD. Nevertheless, fewer studies suggest that MCI-DLB is related to cognitive profile similar to that of MCI-AD, while cognitive scoring alone does not accurately predict MCI-DLB vs MCI-AD. Interestingly, quantitative electroencephalogram may help predicting the progression of MCI to DLB, while preservation of hippocampal volume is associated with increased risk of DLB vs AD, especially in non-amnestic MCI.

Conclusions:: Predicting the progression of MCI to AD or DLB based on neuropsychological profiles is challenging and useful for early therapeutic interventions. More studies are needed, since there are some conflicting findings, while the combination of clinical symptoms with neurocognitive assessment and neuroimaging remains the ideal method for the prediction of MCI progression to various types of dementia.
THERAPEUTIC MODULATION OF NEUROINFLAMMATION IN ALZHEIMER'S DISEASE

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Background and Aims:: Neuroinflammation contributes to the establishment and progression of neurodegenerative diseases including Alzheimer’s Disease (AD). LC3-associated endocytosis (LANDO) protects the brain from aberrant neuroinflammation and is downregulated in AD. Abrogation of LANDO decreases neuroinflammation and AD pathology. Therapeutic intervention targeting neuroinflammation reverses pathology downstream of amyloid deposition, including amelioration of tau-phosphorylation and restoration of memory. Herein, we detail new approaches for targeting neuroinflammation and applicability to human AD therapy.

Methods:: We have utilized two murine models of AD lacking LANDO, one replicating early-onset AD and the second spontaneous age-associated AD. We have utilized two approaches to targeting both NFkB pathway activation and NLRP3-inflammasome activation and have found that NLRP3 inflammasome inhibition alone is therapeutically efficacious using either an established or novel brain-penetrant inhibitor.

Results:: Mice with established disease treated with either of our NLRP3 inflammasome inhibitors displayed robust responsiveness to therapeutic intervention. IL-1b production was suppressed as were decreases in all other inflammatory markers. Tau-hyperphosphorylation was reduced as was activate neurodegeneration. All mice receiving therapeutic intervention had improved memory across multiple analyses.

Conclusions:: The loss of LANDO drives spontaneous AD in mice, and inhibition of neuroinflammation is a potential therapeutic approach for treating neurodegeneration and memory loss. A decline in expression of LANDO regulatory genes in the brains of human AD patients suggests the possibility that a similar mechanism may contribute to disease in human AD and is a viable therapeutic modality in treating AD pathology.
MULTIMODAL EVALUATION OF THE MELANOPSIN RETINAL GANGLION CELLS SYSTEM IN RELATION TO CIRCADIAN RHYTHMS IN ALZHEIMER’S DISEASE AND AGING.

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Background and Aims:: Melanopsin retinal ganglion cells (mRGCs) are deputed to circadian photoentrainment and pupillary light reflex (PLR) regulations. Circadian dysfunction is reported in Alzheimer’s disease (AD) and contributes to dementia. Single-Nucleotide-Polymorphisms (SNPs) in clock genes have been associated to AD.

Methods:: We included 29 mild-moderate AD and 26 matched controls performing neuroophthalmological evaluation including optical coherence tomography (OCT), actigraphic recordings of rest-activity rhythms, chromatic pupillometry and brain functional MRI (fMRI) with light stimulation. 84 clock genes were also analyzed by NGS and relevant single nucleotide polymorphisms (SNPs) validated in a larger cohort of AD (n=449) and controls (n=326).

Results:: In AD disease duration was 3.9±2.8 years and MMSEc score 20.2±4.2. OCT showed a significant reduction of the infero-temporal GCL thickness (p=0.036) in AD. Actigraphy did not disclose significant differences for circadian parameters (IS, IV, RA). However, a subgroup of “circadian-impaired” AD was evident, and most of circadian parameters declined with aging. Pupillometry revealed a significant reduction of PLR peak amplitude in the rod protocol (p=0.006) significantly correlating with aging in AD. Brain fMRI documented the absence of significant responses in AD with sustained blue light stimulation at difference with controls. Genetic analysis in extended AD and control cohorts showed a significant association of the rs30127178 SNP in PER1 gene with AD.

Conclusions:: These results demonstrate, by innovative multi-modal approach, that mRGC system in AD is affected by neurodegeneration. This can be envisaged as a possible biomarker also for conversion from MCI to AD with potential implication for light therapy as a counteracting measure for dementia.
SEX HORMONES AND ALZHEIMER'S DISEASE: A MENDELIAN RANDOMIZATION APPROACH

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Background and Aims:: Sex hormones have been hypothesized to influence AD risk. However, studies of AD based on reproductive characteristics have been inconclusive. Here, we used a Mendelian randomization approach to assess the association between sex steroid hormones (SHBG, Testosterone, Estradiol, and DHEAS) with Alzheimer's disease (AD).

Methods:: We performed MR-egger Mendelian Randomization (MR analysis) using external GWAS summary data to estimate the effects of genetic variants on measured sex hormone levels, stratified by sex. We included independent variants (linkage disequilibrium R²<0.1) and a P-value of 5x10⁻⁸ in the GWAS for sex hormones. Sensitivity analyses included using alternate MR techniques and varying the P-value thresholds.

Results:: Our preliminary findings indicate an association between sex hormone concentrations and AD risk. Specifically, an increased testosterone concentration (per 1 nmol/l) appears to be associated with a decrease in AD risk among women (OR:0.86;95%CI:0.75 – 0.98;P-value 0.03), and possibly among men (OR:0.99;95%CI:0.98 – 1.00;P-value:0.08); and an increase in DHEAS (per 1 umol/l) was associated with a decreased AD risk among the total population (men and women; OR:0.57;95%CI:0.33 – 0.99;P-value 0.05). No associations were found for estradiol and AD, and a possible effect between SHBG and AD among (OR:0.99;95%CI:0.98 – 1.00;P-value 0.09).

Conclusions:: We found an indication that testosterone and DHEAS might have a protective effect on AD. Our findings are limited due to weak instrument bias, especially for estradiol. These preliminary findings indicate sex hormones may influence AD risk, further supporting the hypothesis that sex hormones may be neuroprotective.
ELIGIBILITY FOR DISEASE-MODIFYING TREATMENT IN ALZHEIMER’S DISEASE: EVIDENCE FROM AN OBSERVATIONAL STUDY OVER 4 YEARS

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Background and Aims:: AD diagnosis rarely relies on a pathophysiological marker in memory centers requiring procedure standardisation for real world diagnostic work up. To study the epidemiology of prodromal and mild stages of AD patients who are eligible for clinical trials with disease modifying therapies.

Methods:: We retrospectively analysed data collected at Centre of Dementia and Cognitive Decline, to study the incidence and characteristics of this population eligible for a disease modifying treatment from March 2014 to March 2018. The sample underwent a standardised operational procedure in order to select patients for participation in DMT clinical trials.

Results:: 1143 patients entered the study. Among them, 622 were diagnosed with overt dementia whereas 98 were diagnosed as subjective cognitive impairment and 423 as MCI. Of these, 121/423 (28,6%) were affected by significant somatic comorbidities, 57/301 (18,9%) had a MRI positive for significant cerebrovascular abnormalities, 68/244 (27,8%) patients were lost because of refusals. Among those who were eligible for amyloid biomarker testing 39/177 (22,2%) were negative. A diagnosis of prodromal AD, certified by the use of amyloid-related biomarkers, could be established in 138 (12,1%) out of 1143 patients. By a logistic regression, age, CIRS severity, MTLA, and amnesic MCI were associated with eligibility (p.<001).

Conclusions:: Most patient referred to a Memory Center were not diagnosed at a prodromal stage. Among prodromal AD, most did not fulfil eligibility criteria for entering a disease modifying treatment arguing for the need of more stringent patient journey in the perspective of disease-modifying treatment.
Background and Aims:: Objective: To compare the predictive accuracy of Medial Temporal Lobe Atrophy (MTLA) measurements, for cognitive decline at two-years follow up in subjects subjective memory impairment (SMI).

Methods:: We selected 98 SMI subjects from a memory clinic-based cohort. We clinically assessed all subjects and measured MTLA according to the Scheltens’ visual rating scale. Follow-up was performed annually up to 24 months. Outcome measures were cognitive progression to MCI or dementia. Patients converted to MCI and dementia were assessed by Amyloid PET (Florbetapir).

Results:: Out of 98, 34 SMI subjects progressed to MCI (n= 24) or dementia (n=10) after a 24 months follow-up. Of these, 28 (82%) were positive at Amyloid PET. MTLA measure and APOE genotype but not demographic, clinical and cardiovascular and other somatic risk factors was significantly associated to progression at 12 and 24 months (p<.000), controlling for age.

Conclusions:: according to this study amyloid burden is a common cause of SCI. MTLA and Apoe genotype are useful to predict cognitive decline and amyloid burden in subjects with subjective memory impairment. This may have implications for clinical implementation and screening in the real world.
FTI: A NEUROPSYCHOLOGICAL MARKER TO DISCRIMINATE DIFFERENT CORTICAL FORMS OF DEMENTIA

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Background and Aims: Verbal fluency depends on the linguistic ability to retrieve lexical information (mainly ascribable to the temporal cortex) and on the attentive-executive ability to select several appropriate words (mainly ascribable to the prefrontal cortex). The former ability is especially crucial for semantic fluency, while the latter for phonemic fluency. Therefore, a deficit in phonemic fluency points towards a prefrontal dysfunction, while a deficit in semantic fluency points towards a temporal one. We evaluated whether FTI (Fluency Type Index), a quantitative comparison of performance in the two fluency tasks, functions as a viable parameter to discriminate FTD (Fronto-Temporal Dementia) from AD (Alzheimer’s Disease). Since Tau/Aβ is used with the same purpose, we expected a correlation between FTI and Tau/Aβ in demented patients.

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FTI = \frac{aCF - aLF}{aCF + aLF}
\]

\(aCF =\) adjusted Categorial Fluency
\(aLF =\) adjusted Letter Fluency

Methods: We tested the performance in phonemic and semantic fluency tasks of NC (Normal Controls; n=117) and of patients examined at the UVA of Policlinico Maggiore Hospital, already diagnosed with AD (n=85), bvFTD (behavioral variant FTD; n=48), or aMCI (amnestic Mild Cognitive Impairment; n=97).

Results: The rate of FTI>0 (suggesting a prefrontal impairment) is higher in FTD, while the rate of FTI<0 (suggesting a temporal impairment) is higher in AD \(\left(\chi^2=22.6; df=1; p<0.001\right)\). FTI significantly correlates with Tau/Aβ \(F=3.76; df=1.156; p<0.05\).

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<th>Parameter</th>
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FTI: from -0.22 to +0.50 (calibrated on the NC group)

\( \text{Tau/Ab} \leq 0.52 \)

**Conclusions:** Similarly to Tau/Ab, FTI functions as a (neuropsychological) marker of dementia, capable of distinguishing AD from other neurodegenerative causes of dementia.
PUPILLARY CONSTRICTION VELOCITY AS A BIOMARKER OF BEHAVIOURAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA IN A COHORT OF PATIENTS WITH ALZHEIMER DISEASE

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Background and Aims:: Behavioural and Psychological Symptoms of Dementia (BPSD) represent a huge challenge in Alzheimer’s Disease (AD); commonly, they are assessed through scales administered to the caregiver with a potential subjective bias. The aim of our study was to evaluate the correlation between autonomic parameters and NPI-10 results, in order to find an objective, rapid, and non-invasive biomarker of BPSD

Methods:: N=93 AD patients were recruited (age 78.2 ± 6.1 y.o.; MMSE score 19.5 ± 5.4). Neuropsychiatric Inventory 10-item version (NPI-10) and Caregiver Burden Inventory (CBI) scales were administered to the caregiver; separate symptoms and clusters of NPI-10 were further analyzed. Cohen-Mansfield Agitation Inventory (CMAI) was administered for n=21 patients. Patients and n=28 caregivers underwent assessment of autonomic parameters using Osver ® (Biocubica, Milan, Italy), a polygraphic system able to rapidly measure: pupillary constriction velocity (PCV), frontal temperature (FT), heart rate (HR), perspiration (PER).

Results:: As expected, PCV was lower in AD sample compared to cognitively-spared caregivers (p<0.005 two-tailed Student’s t-test); no differences were observed for FT, HR, PER. Interestingly, PCV decreased to the increase of the NPI-10 score (r=-0.26, p<0.02), and of the CBI (r=-0.28, p<0.01). PCV negatively correlated with the affective cluster (r=-0.38, p<0.002) including anxiety and depression, and with CMAI (r=-0.55, p<0.01), marking agitation. Finally, the anticholinergic burden correlated to PCV (r=-0.25, p<0.02) and HR (r=0.22, p<0.05).

Conclusions:: PCV could represent a potential biomarker of BPSD in general, and of anxiety, depression and agitation symptoms more specifically. Objective measurement of BPSD is necessary in order to guide future therapeutic strategies.
NEUROINFLAMMATION AND BEHAVIORAL DYSFUNCTION: EXPLORING THE ROLE OF DIAZEPAM BINDING INHIBITOR

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Background and Aims:: Alzheimer’s disease (AD) and delirium share common pathogenic mechanisms and neuroinflammation, in particular, represents one plausible candidate link. Diazepam Binding Inhibitor (DBI) is an endogenous ligand of the TSPO receptor, which is expressed by both activated microglia and peripheral monocytes. For this reason, DBI may play a major role in transversely modulating the neuroinflammatory process between the CNS and the periphery. Aim of this preliminary work consisted in assessing DBI serum levels in delirium and AD patients with respect to healthy controls, analyzing particularly behavioral correlates.

Methods:: n=20 not demented patients with delirium were screened by the 4AT scale and recruited from the Neurology ward, together with n=20 matched healthy controls (CTRL) and n=110 AD outpatients without delirium. Serum DBI was assessed by commercial ELISA (AB Frontier).

Results:: DBI serum levels were more than four-fold higher in delirium patients and two-fold higher in AD patients with respect to CTRL (p<0.001). Interestingly, DBI serum levels in AD patients correlated with the Neuropsychiatric Inventory (NPI) total score (r=0.21 p<0.05) and with the Agitation/Aggression NPI subscore (r=0.29 p<0.01). Finally, cognate CSF samples were available from n=23 AD patients: their DBI CSF levels correlated with the serum ones (r=0.50 p<0.05) and with the total-Tau CSF levels (r=0.57 p<0.01).

Conclusions:: Increased DBI serum levels in delirium and AD mark the shared neuroinflammatory landscape both in periphery and the CNS. Notably, DBI levels seem to be increased particularly in agitated patients. Further studies may disclose if serum DBI may be useful as agitation marker in dementia, offering new perspectives for treatments.
ACCELERATED LONG-TERM FORGETTING AS A COGNITIVE MARKER OF SUBJECTIVE MEMORY DECLINE

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Background and Aims:: Subjective memory decline (SMD) is defined as a self-perceived memory decline not detected by standard cognitive testing. SMD may represent the preclinical stage of Alzheimer’s disease (AD) and may underpin initial AD neuropathology. Memory complaints in SMD patients resemble the inter-critical memory failures reported by subjects with epileptic amnesia. In these patients it has been found the Accelerated Long-Term Forgetting (ALF), a defect of the consolidation of memory traces in the post-retention phase, which is usually associated with dysfunctions of the hippocampal regions. The aim of this study is to investigate the presence of ALF in SMD patients.

Methods:: 18 patients with SMD underwent neuropsychological assessment. ALF was evaluated by means of one-week delay trials of Recall and Recognition of the Rey Auditory Verbal Learning Test (RAVLT), Recall of the Rey Complex Figure, and Memory Efficiency Index (a combined score of the RAVLT Recall, Recognition hits and false responses). Results were compared to a matched control group. Mood disorders and memory failures in everyday life were measured respectively by the Depression Anxiety Stress Scale (DASS-21), and the Everyday Memory Questionnaire (EMQ).

Results:: The SMD group performed significantly worse than healthy subjects on verbal memory measures in the one-week delay condition. No correlations were found instead between memory measures and EMQ and DASS-21 scores.

Conclusions:: The SMD patients showed ALF, a defect of the consolidation of memory traces in the post-retention phase. Therefore, ALF might be a useful cognitive marker of SMD and an early sign in the preclinical stage of AD conditions.
CORTICAL NETWORK MODULARITY CHANGES ALONG THE COURSE OF FRONTOTEMPORAL AND ALZHEIMER’S DEMENTING DISEASES

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Background and Aims:: Cortical brain network modularity underpins cognitive functions. We hypothesized its progressive derangement along the course of two neurodegenerative conditions: frontotemporal (FTD) and Alzheimer’s (AD) dementing diseases.

Methods:: EEG was recorded in 18 FTD, 18 AD, and 20 healthy control (HC) matched for age, gender and education. In the FTD and AD patients, the EEG recordings were performed at the prodromal stage of dementia, at the onset of dementia, and three years after the onset of dementia. HC underwent three EEG recordings at 2 to 3-year time interval. Information flows underlying EEG activity recorded at electrode pairs were estimated by means of Mutual Information (MI) analysis. The functional organization of the cortical network was modelled by means of the Graph theory analysis on MI adjacency matrices.

Results:: Graph theory analysis showed that the main hub of HC (left parietal area) was lost in FTD patients at onset of dementia, substituted by provincial hubs in frontal leads. No changes in global network organization were found in AD.

Conclusions:: Despite a progressive cognitive impairment during the FTD and AD progression, only the FTD patients showed a derangement in the cortical network modularity, possibly due to dysfunctions in frontal functional connectivity.
A NEUROPSYCHOLOGICAL STUDY OF AGRAPHIA IN ARABIC IN PATIENTS WITH ALZHEIMER’S DISEASE

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Background and Aims:: Agraphia in Alzheimer’s disease has been widely studied in various occidental languages, but to our knowledge no study has been reported in Arabic language. Methods:: We studied the handwriting’s sample of nine patients with moderate to severe Alzheimer’s disease from the Alzheimer’s Center of Rabat. The average age is 69.2 years (SD: 5.76; 61-77) and of education 12.1 years (SD: 3.3; 6-15), duration of the disease is 4.3 years (SD 2.1; 1-8). Writing samples have been analyzed from MMSE sentence writing. The paragraphias have been analyzed according to the methodology of Caramazza et al, (1987).

Results:: The most frequent paragraphias found are graphomotor patterns (42%), followed by literal substitution (27%), then simple omissions of diacritics (11%). The number of paragraphias was influenced by the level of education, the severity of the diseaes, while age and gender did not have effect. The allographic errors are mainly graphemic simplifications that shared a visuo-spatial similarity with the target letters.

Conclusions:: The graphemic disorders in our patients’ writing are due to an impairment of the peripheral writing processes at probably both graphemic and allographic buffers’ levels (El Alaoui-Faris et al, 2004; McCloskey et al 2018). Furthermore, the missing of diacritics is a typical visuo-spatial feature of the Arabic script.
MUTATIONS IN MME GENE CAUSING DISTAL HEREDITARY MOTOR NEUROPATHY AND MCI-AD

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Background and Aims:: MME gene encodes neprilysin protein(NEP). It is expressed in a wide variety of tissues and it is known to cleave and degrade beta-amyloid. It may have a role in Alzheimer Disease (AD), but it is not yet well understood. Distal hereditary motor neuropathy(dHMN) is a rare cause of neuropathy. MME homozygous mutations cause dHMN. To our knowledge, there are not previous reports of MME dHMN and AD. AIM:Report a patient with dHMN caused by MME homozygous mutation and MCI-AD.

Methods:: 67-year-old healthy woman. At the age of 58, she started with subjective memory loss. On examination MMSE 30/30(GDS2), pes cavus, distal lower limb weakness and atrophy. Her mother suffered from late onset AD. Her brother had axonal motor neuropathy.

Results:: MRI showed an extensive leukoencephalopathy with microangiopathy. EMG: distal axonal motor neuropathy. Toxic-metabolic, infectious, oncologic and immune causes were ruled out. Genetic panel testing of leukoencephalopathy and early-onset dementia was negative. Genetic panel testing for neuropathy showed a pathogenic MME homozygous mutation c.1342C>T(p.Arg448Ter). Her cognitive decline progressed and at 67-years-old, a complete neuropsychological study showed executive dysfunction (GDS3). Biomarkers in CSF were compatible with AD.

Conclusions:: Some studies have investigated relationship between NEP and 1-42 beta-amyloid in AD; it has not been well elucidated, though. There are few cases reported of dHMN caused by MME mutations, but this is, to the best of our knowledge, the first case associated with MCI-AD and CSF-biomarkers. We consider the MME mutations could be the underlying cause of both entities, dHMN and the cognitive decline.
IMPACT OF C9ORF72 AND TARDBP-43 MUTATIONS IN A SARDINIAN COHORT OF FRONTOTEMPORAL DEMENTIA PATIENTS

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Background and Aims:: Sardinians have distinctive genetic characteristics from other Europeans, including mainland Italians. We aim to determine the frequency and the impact of C9orf72 and TARDBP mutations in a Sardinian cohort of FTD patients.

Methods:: Eighty-four patients with frontotemporal dementia (77 unrelated subjects and 7 siblings belonging to three families) were consecutively seen at our Department over a ten-year period (2008 to 2018). FTD diagnosis was made according with the Rascovksy criteria for the bvFTD and the Gorno-Tempini criteria for the PPA. All patients were Sardinian by at least three generations. The following assessments were performed: neurological, neuropsychological, and neuroimaging evaluation, genetic analysis for C9orf72 and TARDBP gene mutations, and family history of FTD and/or ALS.

Results:: Genetic mutations were found in 25 out of 84 patients (30%): 19 carried the GGGGCC hexanucleotide repeat expansion of C9orf72, 5 the p.A382T mutation of TARDBP and 1 carried both mutations. As compared with patients who did not carry any of the investigated mutations, genetic cases were characterized by a lower age at onset (especially in the TDP-43 genotype), and a higher frequency of positive family history (74% of C9orf72 and 100% of TDP-43 mutations). The main clinical phenotype was the bvFTD (69% overall, 100% of C9orf72 and 80% of TDP-43). Compared to non-mutated patients, the C9orf72 showed a higher frequency of parkinsonism (60%) and the TDP-43 of motor-neuron disease (40%).

Conclusions:: Information from our sample confirmed the high frequency of these mutations among Sardinian patients with FTD an their role in clinical presentation and evolution of frontotemporal dementia.
USE OF THE MOROCCAN ARABIC VERSION OF MINI-LINGUISTIC STATE EXAMINATION (MLSE) TO STUDY LANGUAGE DISORDERS IN PATIENTS WITH ALZHEIMER’S DISEASE

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Background and Aims:: The MLSE is a multilingual battery specifically designed to assess language disorders in neurodegenerative diseases. It has been initially developed in English and Italian (Catricalà et al, 2017; Patel et al, 2020). It included eleven tests exploring different language’s domains: motor speech, phonology, semantics, syntax and working memory. We used the Moroccan Arabic version of the MLSE to study language’s disorders in patients with Alzheimer’s disease (AD)(Taiebine, 2021).

Methods:: We study fourteen patients from the Alzheimer Center of Rabat: 4 women and 10 men; 4 with moderate AD and 10 with severe AD. The average age is 68.2 years (SD 6; 57-77), and for education is 13 years (SD 2.9; 6-16). The mean duration of disease is 4.2 years (SD 1.97; 1-8)

Results:: Statistical analysis showed that MLSE scores were mainly influenced by the gender and the severity of the disease, while education level and age had no effect. We found that women performed better than men in semantics, phonology and syntax. There are no difference on motor speech. The marked syntactic deterioration in our patients are probably due to the linguistic structure of Arabic.

Conclusions:: The MLSE opens a new perspective to study language disorders in AD and other neurodegenerative diseases from a cross-linguistic perspective.
FASUDIL PROTECTS NEURONS THROUGH INHIBITING OXIDATIVE STRESS RESPONSE AND RESTORING MITOCHONDRIAL FISSION-FUSION IMBALANCE

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Background and Aims:: The pathogenesis of Alzheimer's disease (AD) is closely related to oxidative stress response and abnormal mitochondrial dynamics. Our previous research demonstrated that Fasudil has neuroprotective effect. Our aim was to explore whether Fasudil has beneficial effect on alleviating oxidative stress and regulating mitochondrial dynamics in APP/PS1 transgenic AD mice.

Methods:: Eight-month-old AD mice were randomly divided into the Fasudil group [i.p. 25 mg/(kg · d)] and normal saline group, and wild-type C57BL/6 mice served as normal controls, once daily for 2 months. Spatial cognition of mice was detected by MWM test and Y maze test. Nissl, TUNEL staining, commercial kits, Western blot, immunofluorescence were applied to observe the neuronal apoptosis, oxidative stress and mitochondrial dynamics.

Results:: Fasudil improved loss of learning, memory and exploration in AD mice. Compared with wild type group, apoptosis of neurons was increased, the expression of Bax and Cleaved Caspase-3 was increased, but Bcl-2 was decreased in AD mice. These changes were strongly reversed by treatment of Fasudil. Furthermore, Fasudil markedly elevated the concentration of antioxidative substances and decreased lipid peroxides, down-regulated the expression of p-DRP1 and FIS1 and up-regulated the expression of OPA1, Mfn1 and Mfn2.

Conclusions:: Fasudil significantly improves the spatial cognition in AD mice, which may be related to restraining oxidative stress and restoring the mitochondrial fission and fusion imbalance, therefore, inhibiting neuronal apoptosis. (NNSF of China 81473577, 81471412, 82004028; Natural Fund Project of Shanxi Province 201901D111334, 201901D211538; Shanxi University of Chinese Medicine 2018TD-012. Ma and Yu are corresponding authors)
PREDICTING COGNITIVE AGE FOR SCREENING FOR NEURODEGENERATION

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Background and Aims:: Machine learning (ML) models can be utilized as a computer-aided detector of accelerated brain aging. We aimed to improve diagnostics of the early cognitive retardation by applying ML approach to psychophysiological and cognitive tests as predictors of age.

Methods:: We used free datasets that describe neurofunctional performance during healthy aging. POBA dataset consists of 231 cases of MRI and psychophysiological examination (reaction time, wrist dynamometry) of people aged 4–83 years. SSCT dataset has tests results (cognitive flexibility, inhibition, updating, and information speed processing) of 103 healthy volunteers in the age range 15-75 years. For the analysis we used ML.

Results:: Reaction time and variance estimates follow a U-shape function that approximates the known inverted U-function of the white matter volume with the optimal values in the early middle-age adulthood (aged 35 years), with a period of stability and accelerated decline only after the late middle age (aged 55-60 years). The shape of the age-related variance of cognitive tests results is close to the straight line. This is similar to the linear trend of the decrease of the gray matter volume.

Conclusions:: Cognitive age can be forecasted from a set of cognitive tests and compared with the actual age. In case of a big difference between the predicted and the actual value, the examinee is susceptible to accelerated brain aging. The performance of ML algorithms identifying subjects’ age groups is better with the cognitive rather than psychophysiological tests as predictors (96.5% versus 94% balanced accuracy; 95% versus 97% sensitivity; 98% versus 86% specificity).
Background and Aims:: The Alzheimer’s Disease Knowledge Scale (ADKS) was developed by Carpenter et al. in 2009 to assess knowledge about Alzheimer’s disease (AD) among general population, caregivers and health professionals. It is composed of 30 items to assess: risk factors, assessment, symptoms, course, life impact, caregiving, and treatment. We translated the Alzheimer’s Disease Knowledge Scale (ADKS) in Arabic to study knowledge about AD in Moroccan population taking into account demographic variables: gender, age, level of education and profession.

Methods:: The sample was consisted of 105 participants (women: 60%), mean age: 41.04 years, (SD:13.30), mean number of years of education (11.42: SD: 2.98).

Results:: The mean total score for the Arabic version of ADKS was 16.59 (SD ± 3.28); it dropped to 14.12 (SD ± 3.05) when excluding health professionals. Individuals with more than 12 years of education and those aged more than 50 years performed significantly well in the ADSK. The best responses were for the following items: course: 64.61%, risk factors: 59.58%, treatment: 61.13% and life impact: 54.03%.

Conclusions:: The use of the Moroccan version of the ADSK allowed us to assess the knowledge of AD among health professionals and general population and to identify the gaps. This allow us to set up appropriate training for professionals and conduct relevant information campaign for the population.
EVALUATION OF THE NEUROPSYCHOLOGICAL PROFILE OF THE ELDERLY POPULATION IN RUSE REGION, BULGARIA

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Background and Aims:: The worldwide population is ageing and the proportion of elderly aged 65 and over is expected to dramatically rise in all the world. In Bulgaria patients with dementia are about 100 000 and their number is progressively increasing. The aim of the present study was to evaluate the neuropsychological and functional profile of patients with cognitive impairment and to compare it with healthy controls.

Methods:: 560 patients with cognitive impairment were prospectively evaluated with a comprehensive neuropsychological battery at Baseline, 6-th, 12-th, 24-th and 36-th month. Patients were recruited from Center for Clinical Neuropsychology and Dementology, Ruse, Bulgaria. A wide range of demographic, clinical and radiological (CT scan of brain) variables were examined, using a matched control group of 75 normal subjects (NCs), as a reference.

Results:: Our results showed significantly poorer performance on MMSE, memory, attention/executive functions and processing speed in patients with cognitive decline in comparison with controls (Fig.1). Significant changes were observed in measures of attention/executive functions, processing speed, short-term and episodic memory and language at follow-up investigations (Fig.2).
Conclusions: Executive functioning deficit appears to have a predictive power for cognitive impairment progression. Among all neuropsychological measures, only Isaac’s Set Test (IST) at 3-rd year follow-up showed significant decline reaching the baseline level impairments in comparison with the results at 12-th month. The executive functioning deficit appears to be the most affected cognitive domain after 3 years of follow-up.
VERTIGO AS UNSPECIFIC DEBUT OF CREUTZFELDT-JAKOB DISEASE: CASE SERIES

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Background and Aims:: Creutzfeldt-Jakob disease (CJD) is a rare neurodegenerative disorder, rapidly progressive and universally fatal, caused by misfolded infectious proteins, called prions. The symptoms of CJD are progressive dementia, myoclonus, depression, psychosis, ataxia, etc. However, it is not clearly reported in the literature what symptom predominates in the debut of the disease.

Methods:: Cases series of six patients diagnosed with CJD, with dizziness as initial symptom.

Results:: Between September 2018 and July 2020, 6 patients (5 women, mean age 58.5) were diagnosed with CJD in our hospital. All patients consulted in the emergency department for dizziness. All of them were treated previously to the diagnosis with anti-vertigo medications, prescribed by their family doctors or by otorhinolaryngologists. On initial physical examination, all patients presented ataxia. Other common symptoms were cognitive alterations (6/6 patients) and myoclonus (4/6 patients). Time to death after diagnosis was between 2 and 5 months. In all patients, 14.3.3 protein resulted positive in cerebrospinal fluid, EEG showed bi-triphasic waves in anterior areas, MRI-brain showed increased signal at b1000 diffusion and SPEC-TC showed hypocaptation in predominantly anterior cortical areas and basal ganglia. Definitive diagnosis of CJD was not possible in any of the six patients, because of rejection of their families of performing autopsies.

Conclusions:: These cases highlight that a very unspecific but common symptom of debut of CJD is dizziness, being the initial and predominant symptom in our cases series. Neurologist should be aware that the debut of CJD can be as unspecific as dizziness, and can be confused with a peripheral vertigo.
ITALIAN CASE REPORT WITH A DOUBLE MUTATION IN PSEN1 (K311R AND E318G)

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Background and Aims:: Alzheimer’s disease (AD) is a progressive and irreversible neurodegenerative disorder that represents the most common dementia worldwide. It’s characterized by deterioration of cognitive skills and of ability to carry out normal daily activities. Most cases of AD are sporadic, but various genetic mutations are known in the literature, which are sometimes associated with clinical, instrumental and laboratory phenotypes not specific of AD. Mutations in PSEN1 are the most common cause of genetic AD. Over 300 different PSEN1 mutations have been identified until now; the majority of these variants are missense mutations, which cause amino acid substitutions. Here we described a double mutation in PSEN1, one of which, never reported in a patient of Italian origin. The two missense variants could modify the role of the protein.

Methods:: Genomic DNA was purified from fresh blood samples by the Salting-out method and a PCR products were sequenced in both directions using BigDye terminator v1.1 chemistry. Human β Amyloid (1-42) ELISA Kit Wako was used for the quantitative determination Aβ (1-42) in CFS sample.

Results:: Here we described a 67-year-old Italian man with Mild Cognitive Impairment (MMSE 24/30) and behavioral alteration, with a double mutation in PSEN 1 (K311R and E318G) but with instrumental investigations (PET, brain MRI and CSF) without evident pathological anomalies.

Conclusions:: This case deepens the role of genetics in pathophysiology of this disabling disease and offers ideas for further investigations. The patient undergoes a clinical, instrumental and laboratory follow-up to see whether he will develop AD.
PREVALENCE RATES OF EARLY ONSET ALZHEIMER’S DISEASE AND FRONTO-TEMPORAL DEMENTIA CLINICAL PHENOTYPES AMONG AGE GROUPS IN THE PROVINCE OF MODENA, ITALY

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Background and Aims:: In a recent study conducted in the province of Modena, Italy, we reported that the most frequent EOD in persons aged 30-64 years was the amnestic variant of AD, followed by the behavioral variant of FTD. Ageing increases prevalence of AD even in patients younger than 65, however, it is not known whether different variants of AD and other causes of EOD are equally affected. Here we studied prevalence of the different clinical variants of EOD by age group.

Methods:: We identified all EOD patients seen in the dementia services of the Modena province, from 2006 to 2019. We included all patients with a diagnosis of dementia with symptom onset before age 65 alive on census date, stratified them according to their age group and computed crude and sex-adjusted prevalence rates.

Results:: Prevalence of all AD showed an exponential growth ranging from 1.8/100,000 in the 40-44 age group to 141.4/100,000 in the 59-64 group. Among AD variants, prevalence of the amnestic variant was the most influenced by the age, while prevalence of PCA and lvPPA showed an almost flat growth curve. Prevalence of all FTD increased linearly from 1.8/100,000 in the 40-44 group to 86.6/100,000 in the 59-64 group, with such increase being all driven by the bvFTD.

Conclusions:: In patients younger than 65, prevalence rates of amnestic AD and bvFTD increase with ageing, while other clinical variants do not seem to show that pattern. These results contribute to a better understanding of the different clinical variants of EOD and their risk factors.
"CREUTZFELDT-JACOB DISEASE OR OTHER RAPIDLY PROGRESSIVE DEMENTIA? DIAGNOSTIC AND PROGNOSTIC VALUE OF EEG, BRAIN MRI AND CSF FEATURES"

Alessandro Castelli, Fabio Placidi, Chiara Giuseppina Bonomi, Claudio Liguori, Andrea Pagano, Luisa Mari, Natalia Manfredi, Nicola Mercuri, Francesca Izzi

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Background and Aims:: The ante-mortem diagnosis of Creutzfeldt-Jacob disease (CJD) is challenging because of resemblance with other rapidly progressive dementia (RPD). Our study aimed to evaluate diagnostic and prognostic value of EEG, brain MRI and cerebrospinal fluid (CSF) features, currently representing CJD diagnostic criteria.

Methods:: a retrospective study on RPD patients admitted at the Neurology Clinic of the University of Rome "Tor Vergata" between 2015-2020. CDC's 2018 Diagnostic Criteria for CJD were applied.

Results:: 13 probable CJD patients and 18 non-CJD RPD patients were included. Periodic sharp wave complexes (PSWCs) were present in 7/13 CJD patients and in 4/18 non-CJD RPD (p=.069). CJD MRI typical patterns were detected in 10/12 CJD and in 2/17 non-CJD RPD (p<.001). 14.3.3 protein was positive in 11/13 CJD and in 1/17 non-CJD RPD (p<.001). A sub-analysis of the CJD group according to EEG features revealed that PSWCs were present in 7/13 patients, non-periodic discharges in 4/13 and focal slowing in 2/13. Compared to patients without PSWC, the average survival time (2.5±0.7 vs 16.6±9.9 months; p=.003) and time to admission (1.4±0.5 vs 8.0±2.5 months; p=.003) were significantly lower in patients with PSWC. As for MRI, CJD patients with PSWC did not show signs of damage on FLAIR images (p=.004).

Conclusions:: In our cohort, EEG showed the weakest specificity among all CJD criteria, but could hold a potential prognostic value since PSWCs were significantly associated with a faster evolution and a reduced survival time. PSWCs might reflect a shorter course of disease, as witnessed by lack of FLAIR signal changes due to astrocytic reactive gliosis.
CORRELATIONS BETWEEN SYSTEMIC COMORBIDITY BURDEN AND CSF BIOMARKERS OF NEURODEGENERATION IN AGING INDIVIDUALS

Henri Zenuni\(^1\), Tommaso Schirinzi\(^2\), Giulia Maria Sancesario\(^3\), Nicola Mercuri\(^2\), Sergio Bernardini\(^2\), Piergiorgio Grillo\(^2\)

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**Background and Aims::** With the worldwide increase of life expectancy, the number of people living with dementia is going to rise dramatically in next years. Since systemic comorbidity is often associated to dementia, increasing the risk, it may represent an ideal target for prevention. In this study we assessed the correlations between systemic comorbidity and CSF biomarkers of neurodegeneration in aging individuals without overt neurological impairment, in order to understand the mechanisms of neuronal vulnerability and offer useful cues for potential neuroprotective interventions.

**Methods::** CSF neurodegeneration-related biomarkers, namely amyloid-β42 (Aβ42), amyloid-β40, total-tau, 181-phosphorylated-tau (p-tau), the Aβ42/p-tau ratio, neurogranin and lactate, of 55 cognitively intact subjects were correlated with the Charlson Comorbidity Index (CCI). The presence of brain lesions was also quantified by the age-related white matter changes (ARWMC) score.

**Results::** In the whole population, CCI had a raw direct association with A42/p-tau and p-tau, and a stronger, age-independent direct correlation with lactate. No correlations resulted with ARWMC score.

**Conclusions::** In normal subjects, systemic comorbidity might reflect at CNS level, affecting the CSF biomarkers profile. Specifically, we observed that concurrent medical conditions can increase oxidative stress (marked by lactate) and, together with aging, contribute to develop an Alzheimer’s disease-like biochemical profile. Although further confirmatory studies on larger samples are now necessary to confirm these preliminary findings, we provided support to neuroprotective strategies based on prevention and cure of systemic diseases.
HYPERCONNECTIVITY IN DEMENTIA IS EARLY AND FOCAL AND VANISHES WITH DISEASE PROGRESSION

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Background and Aims:: In neurodegenerative diseases, including Alzheimer’s disease (AD) and frontotemporal dementia (FTD), functional brain network connectivity is altered, but counter-intuitively is enhanced and defined as hyperconnectivity. What is missing in the literature are data on the evolution of functional connectivity in neurodegeneration; when hyperconnectivity appears along the course of the diseases, and if and how connectivity changes with disease progression. We investigated in a longitudinal multicenter cohort study functional cortical connectivity changes along the course of FTD and AD from the prodromal stage of the diseases.

Methods:: A longitudinal evaluation of EEG activity was recorded in 18 FTD and 18 AD patients at the prodromal stage of dementia, at dementia onset, and 3 years after dementia onset. Twenty healthy controls (HC) underwent EEG recordings at the same time interval as the patients. Mutual information (MI) analysis measured the strength of functional network connectivity.

Results:: FTD and AD patients showed greater MI at the prodromal stage of dementia (FTD vs. HC P=2×10⁻⁸; AD vs. HC P=4×10⁻³). Local connectivity was higher in left and right frontal areas of FTD (P=7×10⁻⁵ and 0.03) and in left and right posterior areas in AD (P=3×10⁻⁵ and 5×10⁻⁵) versus HC.

Conclusions:: We showed cortical hyperconnectivity at the prodromal stage of dementia in areas involved in the specific pathological process of FTD (frontal regions) and AD (posterior regions). Hyperconnectivity disappeared during follow-up, thus suggesting that it is an early electrophysiological feature of dementia, potentially useful to identify prodromal FTD and AD.
Microstructural Damage of White Matter in the Frontal Aslant Tract in Amnestic Mild Cognitive Impairment Subtypes

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1IRCCS Santa Lucia Foundation, Neuroimaging Laboratory, Rome, Italy, 2IRCCS Santa Lucia Foundation, Department Of Clinical And Behavioral Neurology, Rome, Italy, 3University of Sussex, Department Of Neuroscience, Brighton & Sussex Medical School, Brighton, United Kingdom, 4Università Cattolica del Sacro Cuore, Department Of Neuroscience, Rome, Italy, 5University of Torino, Department Of Neuroscience “rita Levi Montalcini”, Turin, Italy

Background and Aims:: Frontal Aslant Tract (FAT) is a bundle connecting Broca’s area to Supplementary Motor Area (SMA) and pre-SMA in both hemispheres, which has been traditionally implicated in speech functions (Catani et al., 2013). A previous study (Serra et al., 2017) showed microstructural damage of FAT in patients with Alzheimer disease (AD) at the stage of dementia. We assessed here microstructural integrity/damage of FAT in patients with amnestic Mild Cognitive Impairment (aMCI) and its potential role in cognitive dysfunctions.

Methods:: Fifty patients with aMCI (25 single-domain [aMCI-SD]; 25 multiple-domain [aMCI-MD]) and 25 healthy subjects (HS) underwent cognitive evaluation and MR scanning at 3T with collection of diffusion imaging data used for probabilistic tractography. FAT was successfully reconstructed in all subjects bilaterally. Microstructural FAT integrity/damage was assessed using fractional anisotropy (FA) maps. Group-comparisons were performed using voxel-wise approach in SPM-8. Mean FA values were used to investigate correlations with patients’ cognitive performance.

Results:: Voxel-wise analysis revealed a bilateral pattern of reduced FA in the FAT of aMCI-MD patients compared to both, aMCI-SD patients and HS. Conversely, aMCI-SD compared to HS did not show any significant difference. Positive associations were found between mean FA from the left FAT and scores at verbal fluency tests in aMCI-SD, and scores at verbal episodic memory tests in aMCI-MD.

Conclusions:: These findings indicate that FAT is bilaterally damaged in AD since the early clinical stage of MCI-MD, thus contributing to the progressive accumulation of cognitive disabilities. Correlations with patients’ cognitive performance suggests a functional role for FAT that goes beyond language abilities.
Background and Aims:: Sundowning, or sundown syndrome, is the emergence or worsening of neuropsychiatric symptoms in late afternoon or early evening in people with dementia. Despite this condition is well known among caregivers and healthcare providers, it has triggered limited scientific interest so far. We aimed to evaluate the prevalence and clinical manifestations of sundowning among patients with dementia and to investigate the clinical and environmental determinants associated with its occurrence.

Methods:: A cross-sectional study of patients with dementia was conducted at the Department of Human Neurosciences of the Sapienza University of Rome between June 2019 and April 2020. The presence of sundowning was investigated through a specifically designed questionnaire administered to caregivers. We compared the sociodemographic and clinical features of sundowners vs. non-sundowners. A logistic regression model was performed to identify the variables associated with sundowning.
Results: Among 152 recruited patients with dementia, 34 exhibited sundowning. The most common manifestations of the sundown syndrome were irritability (15%), agitation (15%) and anxiety (14%). At the univariate analyses, sundowners were significantly older, had more frequent nocturnal awakenings, hearing loss, more severe cognitive, functional and neuropsychiatric impairments and more frequently used medications with an anticholinergic profile and antipsychotics. None of these factors was found to be significantly associated with sundowning at the logistic regression.
CLINICAL MANIFESTATIONS OF SUNDOWNING

- Agitation: 15%
- Irritability: 15%
- Anxiety: 14%
- Delusions: 12%
- Hallucinations: 9%
- Aberrant Motor Behavior: 9%
- Depression: 7%
- Apathy: 7%
- Disinhibition: 4%
- Eating Disorders: 3%
- Other: 3%
- Elation: 2%
Conclusions: Sundowning represents a common neuropsychiatric manifestation among patients with dementia and it appears as a multiply determined condition. Its presence should always be evaluated in the routine practice and a multidimensional approach should be adopted to identify its predictors.

Table 1: Differences between Sundowners and Non-Sundowners at univariate analyses

<table>
<thead>
<tr>
<th></th>
<th>Non-Sundowners (n=118)</th>
<th>Sundowners (n=34)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>78.2 ± 7.6</td>
<td>81.4 ± 6.9</td>
<td>0.03</td>
</tr>
<tr>
<td>Nocturnal Awakenings (n)</td>
<td>1.3 ± 1.6</td>
<td>2.0 ± 2.0</td>
<td>0.04</td>
</tr>
<tr>
<td>CDR</td>
<td>1.8 ± 1.0</td>
<td>2.1 ± 0.8</td>
<td>0.02</td>
</tr>
<tr>
<td>IADL</td>
<td>2.4 ± 2.2</td>
<td>1.1 ± 1.6</td>
<td>0.002</td>
</tr>
<tr>
<td>NPI tot</td>
<td>22.9 ± 16.9</td>
<td>37.0 ± 21.1</td>
<td>0.000</td>
</tr>
<tr>
<td>ACB score</td>
<td>1.1 ± 1.6</td>
<td>2.3 ± 1.6</td>
<td>0.000</td>
</tr>
<tr>
<td>Hearing Loss</td>
<td>33.1%</td>
<td>53.1%</td>
<td>0.04</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>28.2%</td>
<td>60.6%</td>
<td>0.001</td>
</tr>
</tbody>
</table>
FLUENCY TYPE INDEX: A NEUROPSYCHOLOGICAL MARKER TO PREDICT AMNESTIC MILD COGNITIVE IMPAIRMENT PROGRESSION TO ALZHEIMER'S DISEASE.

Claudia Gendarini¹,², Alessandro Cocuzza¹,², Alessandra Romandini¹,², Silvio Mauri¹,², Matteo Mercurio³,⁴, Andrea Arighi³,⁴, Elio Scarpini³,⁴, Giacomo Pietro Comi²,⁵, Maria Cristina Saetti¹,² ¹Fondazione Ca' Granda, IRCCS Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy, ²Dino Ferrari Centre, Neuroscience Section, Department Of Pathophysiology And Transplantation, University Of Milan, Milan, Italy, ³Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurodegenerative Disease Unit, Milan, Italy, ⁴Dino Ferrari Centre, Neuroscience Section, Department Of Biomedical, Surgical And Dental Sciences, University Of Milan, Milan, Italy, ⁵Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neuromuscular And Rare Disease Unit, Milan, Italy

Background and Aims:: Category fluency (CF), mainly dependent on linguistic functions, reveals a temporal dysfunction, while letter fluency (LF), mainly dependent on attentive-executive functions, reveals a prefrontal dysfunction. Fluency Type Index (FTI = adjustedCF – adjustedLF / adjustedCF + adjustedLF) quantifies relative proficiency of each subject on CF and LF. A positive value (FTI+) suggests an attentive-executive deficit and a negative value (FTI-) a semantic deficit, that has been shown to characterize AD.

\[
FTI = \frac{aCF - aLF}{aCF + aLF}
\]

\[
aCF = \text{adjusted CF}
\]

\[
aLF = \text{adjusted LF}
\]

The study aims to investigate FTI’s ability to predict amnestic Mild Cognitive Impairment (MCI) evolution in Alzheimer Disease (AD) and its correlation with a CSF parameter (Tau/Aβ) in aMCI patients.

Methods:: A total of 165 aMCI patients have been divided considering evolution (aMCI-E, n =41) or non-evolution (aMCI-NE, n =124) to AD within 1 year. FTI values and the prevalence of FTI- and FTI+ in each group have been compared. Pearson correlation coefficient between FTI and Tau/Aβ has been calculated and frequency of pathological (< -0.22 and > +0.5) and normal FTI in patients with pathological (> 0.52) and non-pathological Tau/Aβ has been compared with \(\chi^2\) test.

Results:: FTI values are significantly different in the 2 groups (t =2.28, p<.01). In aMCI-E group prevalence of FTI- is higher than FTI+, while no difference emerges in aMCI-NE (\(\chi^2 =5.36\), df =1, p <.05). FTI and Tau/Aβ result negative correlated (r =-0.18, p =0.05). Frequency of pathological/non-pathological FTI and pathological/non-pathological CSF result correlated (\(\chi^2 =3.45\), df =1, p<0.05).

Conclusions:: FTI is a neuropsychological marker that, similarly to T/Aβ, predicts aMCI evolution to AD.
ALZHEIMER’S DISEASE MRI PATTERNS: COGNITIVE, STRUCTURAL AND CEREBROSPINAL FLUID CORRELATES.

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1ASL 3, Neurology Department, Genoa, Italy, 2University of Genoa, Department Of Neuroscience (dinogmi), Genoa, Italy, 3IRCCS, Ospedale Policlinico San Martino, Department Of Neurology, Genova, Italy, 4IRCCS Polyclinic San Martino Hospital, Unit Of Neuroradiology, Genoa, Italy

Background and Aims:: While hippocampal atrophy represents the prototypical MRI finding in Alzheimer’s Disease (AD), other MRI atrophy patterns are commonly found in this population. The differences in clinical and imaging longitudinal evolution associated with the diverse MRI atrophy patterns, however, are poorly understood. Here, we decided to assess the clinical and radiological atrophy progression in AD subjects stratified according to baseline MRI atrophy patterns.

Methods:: 234 amyloid-positive participants with MCI or dementia due to AD from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) with baseline and at least 2-year follow-up MRI scans were included in the study. Subjects were divided in four groups based on the observed MRI-patterns (hippocampal-sparing [HpSpMRI], limbic-predominant [LpMRI], typical-AD [tADMRI], minimal-atrophy [MinAtrMRI]) based on cortical total volume (CTV) and hippocampal volume (HV) values, according to published criteria (Risacher et al., 2017). MRI metrics, clinical outcomes and CSF biomarkers were extracted from the database and compared between the groups at baseline and at 2-year follow-up.

Results:: Compared to other groups, in MCI participants tADMRI and LpMRI showed faster clinical decline than HpSpMRI or MinAtrMRI. At follow-up, 55% of LpMRI patients developed CTV loss and 49 % of MinAtrMRI developed CTV or HV loss. MinAtrMRI patients with a stable MRI pattern had lower baseline total-Tau and phospho-Tau compared to tADMRI and LpMRI.

Conclusions:: In AD, MRI patterns are associated with different clinical and imaging trajectories, suggesting the usefulness of quantitative baseline MRI regional volume evaluation as a possible prognostic marker.
PREVALENCE STUDY OF DEMENTIA WITH LEWY BODIES IN A PARKINSON DISEASE REFERENCE CENTER: CLINICAL AND LABORATORY ANALYSIS OF A RIO DE JANEIRO/ BRAZIL COHORT

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¹Hospital Federal da Lagoa, Neurology, Rio de Janeiro, Brazil, ²Faculdade de Medicina de Campos, Neurology, Campos dos Goytacazes, Brazil

Background and Aims:: Aims: To apply the diagnostic criteria for Dementia with Lewy Bodies (DLB) in a cohort of patients with parkinsonian syndromes in Rio de Janeiro; to estimate the prevalence of this syndrome; to analyze the clinical profile, pharmacological treatment and neuroimaging of this group of patients.

Methods:: Application of the diagnostic criteria for DLB (McKeith, 1996) in patients with parkinsonism and cognitive impairment (after neuropsychological assessment). Selection of patients who met criteria for DLB, clinical and laboratory evaluation of this group.

Results:: 750 patients with parkinsonian syndromes, 22 met the criteria for diagnosing DLB (2.9% of total). Average age 78.36 (SD ± 7.9); 54.5% were men. Mean time neurological symptoms 1.77 years (± SD 0.81). MMSE: 11.3 (SD ± 8.86), MOCA: 9.43 (SD ± 7.2). Domains applied for diagnosis are shown in Table 1. Most prevalent symptoms: bradykinesia (90.9%) and bilateral muscle stiffness (90.9%) [Table 2]. After clinical, laboratory and imaging evaluation, it was concluded that secondary causes were excluded. 100% of cases presented impairment in more than one domain of cognition, impacting their daily activities. Treatment: 18 (81.8%) used levodopa/benseraside, 4 (18%) pramipexole, 13 (59%) quetiapine, 8 (36.5%). MRI morphometric evaluation showed predominance of diffuse cerebral atrophy 21 (95.5%), dilated cerebral ventricles 15 (68.2%), and preservation of temporal lobe structures 17 (77.3%) [Table 3].
<table>
<thead>
<tr>
<th><strong>APPLICATION OF DIAGNOSTIC CRITERIA</strong></th>
<th><strong>N (%)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive impairment impacting daily activities</td>
<td>22/22 (100%)</td>
</tr>
<tr>
<td>Memory impairment</td>
<td>20/22 (90.9%)</td>
</tr>
<tr>
<td>Visuospatial change</td>
<td>20/22 (90.9%)</td>
</tr>
<tr>
<td>Visual hallucinations</td>
<td>18/22 (81.8%)</td>
</tr>
<tr>
<td>Cognitive fluctuations (variation of attention and vigilance)</td>
<td>21/22 (95.5%)</td>
</tr>
<tr>
<td>Spontaneous parkinsonism</td>
<td>19/22 (86.4%)</td>
</tr>
<tr>
<td>REM Sleep disorder</td>
<td>19/22 (86.4%)</td>
</tr>
<tr>
<td>Depression</td>
<td>3/22 (13.6%)</td>
</tr>
<tr>
<td>Other hallucinations</td>
<td>11/22 (50%)</td>
</tr>
<tr>
<td>Sensitivity to neuroleptics</td>
<td>16/22 (76.7%)</td>
</tr>
<tr>
<td>Falls</td>
<td>10/22 (45.5%)</td>
</tr>
<tr>
<td>Syncope</td>
<td>4/22 (18.2%)</td>
</tr>
<tr>
<td>Delirium</td>
<td>11/22 (50%)</td>
</tr>
</tbody>
</table>

Table 1. Diagnostic criteria: domains evaluated. (McKeith et al. 1996)
<table>
<thead>
<tr>
<th>FINDINGS IN CLINICAL NEUROLOGICAL EVALUATION</th>
<th>N(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRADYKINESIA</td>
<td>20/22 (90,9%)</td>
</tr>
<tr>
<td>MUSCLE STIFFNESS</td>
<td>20/22 (90,9%)</td>
</tr>
<tr>
<td>REST TREMOR</td>
<td>16/22 (72,7%)</td>
</tr>
<tr>
<td>ALTERED POSTURAL REFLEX</td>
<td>15/22 (68,2%)</td>
</tr>
<tr>
<td>PYRAMIDAL MOTOR DEFICIT</td>
<td>0/22 (0%)</td>
</tr>
<tr>
<td>SPHINCTER RELEASE</td>
<td>1/22 (4,5%)</td>
</tr>
</tbody>
</table>

Table 2. Neurological Evaluation in a series of patients treated.
Conclusions:: Prevalence of 2.9/100 DLB patients in this cohort. Significant cognitive impairment with few years of evolution, predominance of rigidity and bradykinesia on neurological examination and clinical manifestation started in the seventh decade of life were more specific results found.

<table>
<thead>
<tr>
<th>NEUROIMAGING FINDINGS</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preservation of Temporal Lobe Structures</td>
<td>17 (77,3%)</td>
</tr>
<tr>
<td>Hippocampal Atrophy</td>
<td>4 (18,2%)</td>
</tr>
<tr>
<td>Diffuse brain atrophy</td>
<td>21 (95,5%)</td>
</tr>
<tr>
<td>Ventricular enlargement</td>
<td>15 (68,2%)</td>
</tr>
<tr>
<td>Microangiopathy</td>
<td>13 (59,1%)</td>
</tr>
<tr>
<td>Acute ischemic disease</td>
<td>2 (9,1%)</td>
</tr>
</tbody>
</table>

Table 3. MRI morphometric evaluation.
A CHALLENGING DIAGNOSIS OF NEURODEGENERATIVE DEMENTIA: PSYCHIATRIC ONSET OF FRONTOTEMPORAL LOBAR DEGENERATION

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Background and Aims:: Frontotemporal lobar degeneration (FTLD) is a heterogeneous syndrome characterized by degeneration of the frontotemporal lobes associated with language, executive, and behavioral disturbances. Psychiatric symptoms have been reported over the disease course. When presenting at the onset, diagnosis can be highly challenging. We report three unusual cases of FTLD with psychiatric onset.

Methods:: Case1. A 69-year-old man presented with a late-onset major depressive disorder, lasting for two years slightly improved by antidepressant therapy; when developing progressive effortful and agrammatic speech, he underwent brain MRI showing left posterior frontal and insular atrophy. Case2. A 49-year-old woman with a one-year history of religious delusion complained of attentive and memory disturbances associated with socially inappropriate behaviors; brain MRI showed mild atrophy in the bilateral frontotemporal regions. Case3. A 63-year-old woman without a history of eating disorders had significant weight loss, associated with progressive language deterioration; brain FDG-PET revealed severe hypometabolism in left frontotemporal regions. All cases underwent CSF analysis or amyloid-PET.

Results:: Case1 received a diagnosis of progressive non-fluent aphasia, manifesting at the onset with depression. Case2 was diagnosed as a behavioral-variant of frontotemporal dementia. Case3 received a diagnosis of semantic dementia, with anorexia nervosa at the onset.

Conclusions:: Clinical differentiation of neurodegenerative dementia from a primary psychiatric disorder may be challenging, especially in FTLD with psychiatric onset. Neurodegenerative disorders should be suspected when a late-onset psychiatric disorder is associated with inadequate treatment response and cognitive deficits. Accurate clinical evaluation, CSF analysis, and neuroimaging are the main weapons for a physician.
CORTICAL BASAL SYNDROME IN A PATIENT WITH A CLINICAL AND PATHOLOGICAL OVERLAP BETWEEN TAUOPATHY AND SYNUCLEINOPATHY. EVIDENCE FROM THE TREDEM REGISTRY

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Background and Aims:: An 82-year-old male right-handed retired teacher reported in 2019, that three years earlier he developed difficulties in moving his left arm and foot, tremor in left-hand and gestures of the left upper limb that appeared to be independent of the patient's will, characteristics of alien limb phenomenon. We present a patient with cortical basal syndrome (CBS) and amnestic MCI who showed the presence of α-synuclein aggregates in the CSF and in the olfactory mucosa samples.

Methods:: A clinical, neuropsychological, imaging and biomarker evaluation, including tau and amyloid proteins levels in the CSF and RT-QuIC assay for α-synuclein both in the CSF and olfactory mucosa, was conducted

Results:: At neurological examination the patient, on the left side, presented with resting tremor, mild extrapiramidal hypertonus, mild bradykinesia and severe apraxia on the left upper limb. Brain MRI showed a knife-edge posterior parietal cortical atrophy prevalent on the right hemisphere. 18F-FDG PET imaging showed hypometabolism of the right lateral parietal, temporal cortex, precuneus and posterior cingulate cortex. The DaTscan showed a mild thinning of the right putamen. Neuropsychological tests showed memory and visual-perceptual deficits. CSF tau and amyloid measurements did not show clearly pathological values (Tau protein 395 pg/ml; ratio Abeta42/P-Tau181: 6.8) while RT-QuIC for α-synuclein in CSF and olfactory mucosa samples were positive.

Conclusions:: Although in our patient the clinical diagnosis was of probable CBS, usually expression of tauopathies, unexpectedly RT-QuIC detected α-synuclein aggregates showing a probable α-synuclein pathology. RT-QuIC provides a better definition of underlying pathologies in neurodegenerative disorders with prognostic and potentially therapeutic implications.
COMPARISON OF PLASMATIC INTERLEUKINS PATTERNS AMONG COGNITIVELY UNIMPAIRED SUBJECTS, PATIENTS AFFECTED BY MILD COGNITIVE IMPAIRMENT AND SUBJECTS WITH ALZHEIMER’S DISEASE DEMENTIA

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Background and Aims:: We investigated a panel of plasma interleukins (ILs) levels hypothesized to play a role in aging and AD pathophysiology, in a pooled cohort of clinically characterized (according to NIA-AA core clinical criteria) cognitively unimpaired (HC), Mild Cognitive Impairment (MCI), and Alzheimer’s Disease Dementia (ADD) individuals.

Methods:: In 137 subjects (43HC, 63MCI and 31ADD), the plasma levels of IL1-β, IL-6, IL-10, IL-12, IL-6 receptor (IL-6R), TNF-a and TGF-b were measured by ELISA kits on samples collected at 8.00 AM and quickly frozen. Principal component analysis (PCA) was performed as the initial exploratory step; parametric statistic was assessed to evaluate group differences and association between IL and biological factors (age, sex, APOEe4). An exploratory clustering approach was carried out to investigate distinct biological profiles.

Results:: In the total sample, IL12 was positively associated with age. We found a positive association between IL1β and IL12 and female sex and between IL12 and APOEe4 allele. MCI individuals, but not ADD patients, had higher concentrations of IL10 than HC. K-means clustering (k=3) showed a cluster predominately characterized by ADD over the other two populations and lower IL12 and IL10 than the other two clusters. A component, mainly characterized by the IL-6R was negatively associated with MMSE.

Conclusions:: Our preliminary results indicate a potential effect of critical biological factors such as aging, sex, and APOEe4 allele on some ILs hypothesized to be critical orchestrators of neuroinflammation. Speculative hypotheses based on translational data, are drawn upon the clusters found. Our results, support the investigation of IL-based profiles of neuroinflammation in AD.

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LEXICAL-SEMANTIC SYSTEM DISRUPTION CORRELATION WITH ALZHEIMER’S PATHOPHYSIOLOGICAL PROCESSES

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Background and Aims:: Semantic cognition is early affected in Alzheimer’s disease (AD), but its relationship with AD neuropathological hallmarks burden (i.e. amyloidosis, A; tauopathy, T; neurodegeneration, N) is controversial. We addressed this issue investigating the relationship between non-traditional semantic neurolinguistic metrics and AD pathology.

Methods:: Median typicality (TYP) and frequency of use (FU) of words produced in a semantic verbal fluency (SVF) task were assessed in a sample of 49 (AD n=29, non-AD, NAD, n=20) consecutive non-aphasic neurodegenerative patients who consented to CSF ATN biomarker assessment for categorization as per ATN system (NIA-AA 2018 criteria). The exploratory outcomes were: 1) differences in median TYP and/or FU between AD vs NAD groups; 2) correlation between median TYP and FU with CSF ATN biomarkers in AD vs NAD.

Results:: Median TYP and FU were found significantly higher in AD than in the NAD group only when A⁺T⁺ patients (n=22) were considered, while grouping them with the highly variable performances of A⁺T⁻ patients (n=7) diluted this difference to non-significance. No significant correlation with CSF biomarkers were detectable in the NAD group; conversely, in the AD group as a whole (n=29), TYP and FU inversely correlated with ABeta1-42/1-40 ratio and positively with tTau and pTau.

Conclusions:: Semantic competencies could vary widely at the earlier AD neuropathological stages (A⁺T⁻), but they seem to get worse with advancing tauopathy (A⁺T⁺), distinguishing this AD stage from NAD conditions and, consistently, correlating with A, T and N CSF biomarkers only in AD spectrum, acting as a putative proxy for ongoing AD pathophysiology.
EEG ABNORMALITIES IN PATIENTS WITH DELIRIUM AS A PREDICTIVE BIOMARKER OF DEMENTIA WITH LEWY BODIES

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Background and Aims:: Delirium is an acute neurological dysfunction, characterized by altered conscious state, akin to fluctuating cognition. It is frequent in elderly patients when hospitalized and is characterized by an increased risk of developing dementia, especially Dementia with Lewy Bodies (DLB). EEG Prominent posterior slow-wave activity in the pre-alpha/theta range is a supportive biomarker for DLB diagnosis from the prodromal stage. This EEG pattern correlates with fluctuating cognition and is the electrophysiological underpinning of the so-called thalamo-cortical dysrhythmia. We aim to assess whether non-demented hospitalized patients with delirium show specific QEEG abnormalities typical of thalamo-cortical dysrhythmia.

Methods:: 24 consecutive patients admitted to Neurology Clinic of University of Chieti were administered Mini Mental State Examination (MMSE) as per clinical routine. The presence of delirium was assessed by 4AT test. All subjects underwent resting state EEG recording.

Results:: 11 (7 females) presented delirium (delirium, D) according to 4AT (9 with hypokinetic, 2 with hyperkinetic type), 13 (5 females) did not show it (controls, C). The two groups did not differ for age and gender. In all but one D (91%), we observed alterations of EEG parameters (DF lower than alpha with increased DFV (>1.2 Hz)). In C, DF and DFV were normal in 92%, (alpha DF and DFV<1.2 Hz) (DF in D vs. C p=0.002).

Conclusions:: We found strong correlation between the presence of delirium and EEG abnormalities typical of thalamocortical dysrhythmia and of DLB. Our evidence suggests a pathophysiological explanation for delirium. EEG may represent a powerful tool to detect delirium.
A VITAMIN B12 DEFICIENCY PRESENTING WITH CLINICAL, LABORATORY AND RADIOLOGICAL FEATURES OF PRION DISEASE

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Background and Aims:: Rapidly progressive dementias (RPDs) are severe cognitive impairments occurring over weeks to months. Prion disease is one of the most common cause of RPD. We report the case of a subject with RPD due to vitamin B12 deficiency mimicking prion disease.

Methods:: A 70-year-old man presented with rapidly progressive cognitive deterioration and behavioral changes starting 6 months before. Neurological evaluation showed sensory deficit and ataxia. The patient was disoriented and displayed severe verbal fluency reduction. Brain MRI showed hyperintensities of the heads of caudate nuclei and the left insular cortex in DWI (Figure A). The EEG showed diffuse non-specific slowing. Total-body CT were negative. A positive 14-3-3 protein in the CSF was found while RT-Quic resulted negative. The hypothesis of sporadic Creutzfeldt-Jakob Disease (sCJD) was then posed. Serum analysis demonstrated macrocitic anemia with hyperhomocysteinemia and low vitamin B12.

Results:: Supplementation therapy was then initiated. Two months later, neuroimaging, laboratory testing and neurological examination were unremarkable remaining stable at 12-months follow-up (Figure B). Thus, the diagnosis of dementia secondary to vitamin B12 deficiency was made.

Conclusions:: To our knowledge, this is the first report of vitamin B12 deficiency presenting with RPD, ataxia, DWI telencephalic gray matter alterations and 14-3-3 positivity. Vitamin B12 deficiency was not reported as a typical MRI mimic of sCJD. Furthermore, studies in rodents demonstrated CSF prion protein may occur in vitamin B12 deficiency. This case demonstrates the variability of vitamin B12 deficiency manifestations and underscores the importance for screening and management even in atypical presentations, considering the reversibility of abnormalities.
THE SCOT PROJECT: A MULTI-COMPONENTIAL INTERVENTION TO REDUCE LONELINESS IN THE ELDERLY POPULATION

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Background and Aims:: Social isolation and reduced involvement in cognitive activities are associated with an impact on cognitive well-being and health status in elderly adults. In particular, loneliness and social isolation represent risk factors in favouring cognitive decline and dementia. Here, we present the study design and baseline features of the Social Cognition Online Training (SCOT) project, aimed to evaluate the beneficial effects of an online intervention on social-cognitive functioning in healthy elderly subjects.

Methods:: The study include 60 cognitively healthy elderly subjects. Subjects were randomly assigned to the experimental (SCOT) or the active control group. SCOT training was focused on reducing loneliness (i.e., improving social skills, increasing social contact, addressing maladaptive social cognition) and on promoting cognitive stimulation (i.e., executive functions). Outcome measures were the Italians’ Social and Emotional Loneliness Scale (ISELS), a new developed task of complex emotion recognition (EMOTI-COM) and the Tower of London (ToL).

Results:: Preliminary analysis on the first 27 enrolled subjects showed no significant differences between the SCOT and the control group in sex ($\chi^2(1)=0.03$, $p=0.8$), age ($t(25)=0.4$, $p=0.7$) and education ($t(25)=0.2$, $p=0.8$). No differences were found between groups at baseline in the outcome measures (EMOTI-COM: $t(25)=-0.439$, $p=0.6$, ISELS ($t(25)=-0.003$, $p=0.9$, ToL Accuracy: $t(25)=-1.970$, $p=0.06$).

Conclusions:: The development of interventions to prevent and delay cognitive decline represents a priority in an ageing World. If the SCOT program will prove an effect in promoting social well-being in ageing, this will represent the first step in the introduction of new preventive programs.
A MACHINE LEARNING-BASED HOLISTIC AND AGE-DEPENDENT APPROACH FOR THE DIAGNOSIS WITHIN THE ALZHEIMER'S DISEASE SPECTRUM

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Background and Aims:: Alzheimer’s disease (AD) is a neurodegenerative condition driven by a multifactorial etiology. No disease-modifying strategies are available and almost all the AD clinical trials have failed. However, a growing body of evidence indicates that early prevention strategies may delay AD onset and progression. The development of cost-effective approaches set to identify subjects at-risk of developing AD is, thus, critical.

Methods:: In this study, we employed a machine learning (ML) based algorithm and the wealth of information offered by the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database to investigate the contribution of clinically relevant factors for identifying subjects affected by Mild Cognitive Impairment (MCI), a transitional status between healthy aging and dementia.

Results:: Our ML-based algorithm did not help to predict the conversion of MCI subjects to AD. On the other hand, non-converting (ncMCI) subjects were correctly classified and predicted. Two neuropsychological tests, the FAQ and ADAS13, were the most relevant features used for the classification and prediction of younger, under 70, ncMCI subjects. Structural MRI data combined with systemic parameters and the cardiovascular status were instead the driving factors for the classification of over 70 ncMCI subjects.

Conclusions:: Our results support the notion that AD is not an organ-specific condition and results from pathological processes inside and outside the brain. In addition, the study, by exploiting the unbiased computational capability offered by artificial intelligence-based approaches, provides a tool to understand the unique complexity of “individual” diseases affecting patients, thereby helping to take full advantage of precision medicine in the diagnosis and treatment of dementia.
Background and Aims:: According to the WHO today about 422 million people worldwide have diabetes and chronic course of diabetes leads over time to decrease the cognitive functions and the development of dementia. The aim of this study was to decipher neuromorphological changes in type 2 diabetes that potentially affect cognitive impairment.

Methods:: We have performed a clinical-morphological comparison of outpatient card data, disease histories and autopsy reports of 15 cases of type 2 diabetes.

Results:: The main cyto-angio-architectonic manifestations of diabetic brain damage are diffuse alteration of the basement membranes and vascular endothelium, capillary fibrosis and hyalinosis, pericyte proliferation, congophilic angiopathy accompanied by a sharp disruption on transcapillary transport. There is a combination of acute and chronic processes, reversible and irreversible changes in nerve cells: neuronal swelling, subtotal chromatolysis, karyopyknosis and cytoplasmic homogenization, satellite disease, perikaryon enlightenment, tigrolysis, lysis of neurons with the formation of "shadow cells". In areas of chronic ischemia there are neurons or groups of neurons with morphological signs of Alzheimer's neurodegeneration (pathological neurofibrils in the form of tangles), a large number of hematoxylin spheres and single Lafora bodies. Moreover, single terminal plaques are found in the impregnation of silver by the Bielschowsky staining method.

Conclusions:: Thus, the brain morphological changes in type 2 diabetes mellitus are formation neurofibrillary tangles are thought to contribute to the degradation of the neurons in the brain, congophilic angiopathy of small vessels and vessels of medium caliber. The combination of vascular and neurodegenerative components can mutually potentiate each other, causing clinical symptoms of cognitive deficits.
Background and Aims:: Binswanger disease or subcortical arteriosclerotic encephalopathy refers to slowly progressive white-matter vascular dementia. Patients usually present symptoms including forgetfulness, personality and emotional changes. The aim of this study was to investigate the neuropathological substrates of cognitive impairment and dementia in Binswanger disease for the reliability of the diagnosis.

Methods:: Seven patients with a clinical diagnosis of microangiopathic encephalopathy of Binswanger and cognition impairment were studied. The gross examination and microscopic study of brain tissue were done.

Results:: White matter pathology was accompanied ventricular enlargement and lacunar infarcts in the basal ganglia and thalamus. Gross pathology showed variable involvement of the white matter, which may be superficial and subcortical or extend deep into the white matter to periventricular sites. Microscopical changes were two types of capillaropathy, mainly subcortical structures: obstruction of the lumen of the vessel and capillary stagnation as a result of chronic "retrograde venous support", due to which the blood filling of the vessels remains at a relatively high level. Both types are accompanied by diffuse ischemia of the white subcortical substance and by the development to many pericapillary microinfarctions. The genesis of dementia in Binswanger's encephalopathy is associated with "disconnection-syndrom", with the separation of cortical subcortical connections as a result subcortical white matter damage, and with dysfunction of the basal ganglia and thalamus.

Conclusions:: Binswanger disease is characterised by arteriolosclerosis, lacunar infarcts and diffuse white matter changes with myelin loss, axonal abnormalities and evidence of neuropathological cognitive impairment and dementia.
MILD COGNITIVE IMPAIRMENT DUE TO PRIMARY PROGRESSIVE APHASIA: A NEUROPSYCHOLOGICAL AND NEUROIMAGING 9 YEARS-FOLLOW UP CASE REPORT.

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Background and Aims:: Mild Cognitive Impairment (MCI) is a heterogenous clinical entity, that may represent the initial phase of different type of neurodegenerative disorders. Our aim is to elucidate the early phases of clinically suspect Primary Progressive Aphasia (PPA) in order to better focus the presenting neuropsychological profile for earlier diagnosis.

Methods:: Neuropsychological tests, language evaluation, brain morpho-functional imaging and cerebrospinal fluid (CSF) analysis allowed to diagnose a MCI converted to Semantic variant Primary Progressive Aphasia (SvPPA).

Results:: Disease onset was at age 69 years with memory impairment and word finding difficulty. First neuropsychological evaluation resulted in non-amnestic MCI (fluency and visuo-spatial skills deficiency). After seven years of clinical follow up, the patient presented behavioral disturbances and cognitive worsening. Brain magnetic resonance imaging showed left inferior, medial and anterior temporal atrophy. Fluorodeoxyglucose positron emission tomography (FDG-PET) scans of the brain evidenced left anterior temporal and anterior cingulate cortex hypometabolism. Amyloid-PET resulted negative. CSF tau and phospho-tau resulted increased. Detailed language testing revealed marked difficulty with confrontation naming, moderate improvement after cueing, word substitutions, circumlocution, impaired comprehension (token test), but spared speech, grammar and repetition. So that, he converted to Semantic variant Primary Progressive Aphasia.

Conclusions:: Primary Progressive Aphasia, like other progressive neurodegenerative diseases, can pass through an early (MCI) phase prior to the dementia phase. Clinical use of CSF and imaging biomarkers are of a great value in MCI etiopathogenetic differential diagnosis process. Our case suggests that earlier language evaluation may be a helpful tool especially in clinical evaluation of amyloid-negative patients associated to advanced neuroimaging.
THE EFFECT OF TRINUCLEOTIDE REPEATS IN THE HTT GENE ON THE PROGRESSION FROM SUBJECTIVE COGNITIVE DECLINE TO MILD COGNITIVE IMPAIRMENT: A 12 YEARS FOLLOW-UP STUDY

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Background and Aims:: Intermediate alleles (IA) of HTT gene occurs for CAG triplet repeats between 27 and 35. IA seem to play a role in the pathogenesis of Alzheimer’s disease. The aim of our study was to assess the effect of IA on progression from Subjective Cognitive Decline (SCD) to Mild Cognitive Impairment (MCI).

Methods:: We enrolled 120 SCD patients. All patients underwent extensive neuropsychological assessment, estimation of premorbid intelligence, a proxy of cognitive reserve, APOE and HTT genes genotyping and neuropsychological follow-up every 6-12 months.

Results:: Ten patients (8.33%) were carriers of IA (IA+). During follow-up 39 patients progressed to MCI (p-SCD) in a mean time of 13.96 (± 6.56) years, while 81 remain stable (np-SCD) in mean follow-up time of 11.06 (± 7.55) years. A regression analysis considering progression to MCI as dependent variable and age at onset of SCD, cognitive reserve proxies, APOE genotype and IA showed that APOE e4 was the only significant variable in the predictive model. Therefore, we stratified the sample according to APOE genotype. In the e4 carrier group we found that IA+ patients had twice as high risk of progression to MCI compared to IA- patients. We also stratified the the sample by age at onset >60 years. In patients older than 60, IA+ had 1.84 times higher risk of progression to MCI compared to IA-.

Conclusions:: Our results suggest that IA of the HTT gene interact with age at onset of SCD and with APOE genotype increasing the risk of progression from SCD to MCI.
DOES APOE 2 POLYMORPHISM PLAY A PROTECTIVE ROLE AGAINST ALZHEIMER'S DISEASE?

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Background and Aims:: Human apolipoprotein E (ApoE) genotype is the only confirmed genetic risk factor for Alzheimer’s disease. As the most common isoform, ApoE3 is believed to play a neutral role in AD, while ApoE4 exists in nearly 50% of AD patients. On the other hand ApoE2 is relatively rare and is considered to be a protective variant against AD via its effects on Amyloid beta metabolism. In this retrospective longitudinal study we analyzed a population inside of the AD continuum to investigate the effect of these Epsilon variants on the CSF biomarkers trending levels.

Methods:: We evaluate over 140 subjects, came in the Memory Clinic of Policlinico Tor Vergata (Rome), suffering one year history of memory deficit due to recent events or subjective one. Patients underwent neuropsychological assessment, ApoE genotyping and lumbar puncture to evaluate CSF biomarkers (Abeta-42, T-Tau, P-Tau) for diagnostic purposes.

Results:: Individuals with AD continuum and ApoE2 polymorphism despite the absence of tau pathology in CSF show different T-Tau levels then controls. Particularly ApoE2 subjects having neurodegeneration signs documented with T-Tau/Abeta42 and P-Tau/Abeta42 ratios didn't showed difference with ApoE3 and ApoE4 patients in terms of CSF biomarkers levels and neuropsychological scores, indicating some detrimental mecanism of epsilon 2 isoform still unknown.

Conclusions:: ApoE2 genotype role in the pathogenesis of AD has to be investigated yet and could give counteracting effects on the course of Alzheimer’s disease, especially in the presents of lesional load indices and initial Tau pathology. Its protective effects might vary with the stage of AD.
THE NEW SUDAN COGNITIVE ASSESSMENT TOOL (SUCAT) IS A POTENTIAL _EARLY DETECTOR FOR LOW-INCOME COUNTRIES _THAT SURPASSES THE _LIMITATIONS OF MMSE AND MOCA

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Background and Aims:: Dementia is characterized by a decline in one or more cognitive domains; WHO listed Alzheimer/Dementia accounts for 4,756 deaths (1.78% of 41.8 million in the total population, 2018 census) In Sudan, where the research proved the unsuitability Mini-Mental State Exam (MMSE) and the Montreal Cognitive Assessment (MoCA) to detect Mild Cognitive Impairment (MCI). This is based on the diversity of Sudan’s cultural, educational, and linguistic background where Arabic with three informal dialects (colloquial Arabic; El-Darigia الدارجية) is used. Moreover, they are literate dependant. Hence, SuCAT is developed to test the known SEVEN cognitive domains.

Methods:: This analytical cross-sectional study composed of four piloting and validation phases.

Results:: Phase I; two studies; the first concluded that the Arabic version of the MMSE was not suitable for Sudan, while the second showed that MoCA and MMSE scores have a strong association with educational level (P. value = 0.000). Phase II was conducted as a pilot test of the validity and reliability of SuCAT as Literacy independent adapted Arabic version. It concluded that SuCAT is a potential test for cognitive impairment among Sudanese patients. Phase three was for SuCAT standardization at a larger, in which it was found to significantly surpass MMSE and MoCA in five of the seven domains, neutral in one and inferior in “Coping” (P. value = 0.000). Phase IV is to validate SuCAT for certain cognitive disorders.

Conclusions:: In conclusion, SuCAT is a promising Neuropsychological test with expected good health impact in a low-income country like Sudan. This might pave the way for similar countries worldwide.
7,8-DIHYDROXYFLAVONE ATTENUATES COGNITIVE DEFICIT IN ICV-STZ RAT MODEL OF ALZHEIMER’S DISEASE REVERSING OXIDATIVE STRESS, MITOCHONDRIAL DYSFUNCTION, AND INSULIN RESISTANCE

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Background and Aims:: Sporadic Alzheimer’s disease (SAD) is the most commonly prevalent dementia and progressive neurodegenerative disease. A polyphenolic flavonoid, 7,8-dihydroxyflavone (7,8-DHF) was used to reverse the cognitive deficit in a rat SAD model by reversing oxidative imbalance, mitochondrial enzyme dysfunction, and insulin resistance.

Methods:: For the SAD model, streptozotocin (STZ-3 mg/kg) was injected intracerebroventricularly (ICV) in male Wistar rats to induce cognitive dysfunction. Cognitive functions were evaluated by Morris water maze (MWM) and novel object recognition (NOR) tests, while locomotor activity was determined in actophotometer. 7,8-DHF was given orally in doses of 5 mg/kg, 10 mg/kg, and 20 mg/kg, and reference standard drug rivastigmine in a dose of 2 mg/kg. Antioxidant enzymes, mitochondrial enzyme complexes were determined biochemically, insulin-degrading enzyme (IDE) and p-tau by ELISA, and histopathology by H&E staining.

Results:: 7,8-DHF attenuated cognitive deficit induced by ICV-STZ in MWM and NOR. Moreover, in the cortex and hippocampus regions of the brain, levels of reduced glutathione, catalase, superoxide dismutase, and mitochondrial complex enzymes and increased lipid peroxidation, protein carbonylation, and nitrite levels were subsequently reversed by 7,8-DHF and rivastigmine. IDE and p-tau protein were found to be altered. Histopathological examination revealed halted neurodegeneration.

Conclusions:: Conclusively, 7,8-DHF was found to be neuroprotective in the ICV-STZ rat model of SAD by ameliorating oxidative stress, mitochondrial dysfunction, and insulin resistance, thereby improving cognitive functions evident with the behavioral results. Hence, these results can further have clinical relevance in human AD.
ALTERATIONS OF INWARDLY RECTIFYING POTASSIUM CHANNELS AN AB(1–42)-INFUSED RAT MODEL OF ALZHEIMER’S DISEASE

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Background and Aims:: Alzheimer’s disease (AD) represents the most common form of dementia in elderly individuals. AD is clinically characterized by irreversible and progressive neurodegeneration leading to memory deterioration, behavioral changes and cognitive dysfunction. Despite its prevalence, the AD pathogenesis is not completely understood, and, currently, there are no effective treatments to slow or halt the progression of its symptoms. Emerging studies reported that a dysfunction of ion channels is associated with the pathophysiology of a wide range of neurological disorders, including AD. Among them, the inwardly rectifying potassium (K+) channels (Kir) play a key role in the maintenance of the resting membrane potential and in the regulation of cell excitability by the controlling of the intracellular and extracellular flow of K+ ions. Therefore, the aim of the study was to investigate the role of neuronal Kir channels in AD pathophysiology.

Methods:: The mRNA and protein levels of neuronal Kir2.1, Kir3.1, and Kir6.2 were determined by quantitative real-time PCR (RT-qPCR) and Western blot analysis in the hippocampus of an amyloid-β(Aβ)(1-42)-infused rat model of AD. Extracellular deposition of Aβ was confirmed by both histological Congo red staining and immunofluorescence analysis.

Results:: Significant decreased mRNA and protein levels of Kir2.1 and Kir6.2 channels have been observed in the hippocampus of the rat model of AD, whereas no differences were found in Kir3.1 channel levels as compared with controls.

Conclusions:: Data corroborated the hypothesis that Aβ can modulate the expression of Kir channels, which may represent potential therapeutic targets in the AD treatment.
DIFFERING GLIAL EXPRESSION PROFILES AS A MEANINGFUL MEASURE OF EARLIEST STAGES OF ALZHEIMER’S DISEASE (AD) PATHOGENESIS

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Background and Aims:: Neuroinflammatory dysfunction is a well-known phenomenon encountered in brains of demented AD individuals, but little is known about its role in earliest stages of AD pathogenesis. We assessed glial immunoreactivity in brain regions where tau burden was just about to develop and evaluated differing expression profiles in cognitively diverging individuals.

Methods:: We performed immunohistochemical analysis and stereological cell-quantifications in brain tissue of demented and non-demented subjects who harboured identical tau burden (Braak III/IV) evaluating brain regions temporally matched to this incipient tau acquisition (temporal pole, occipital cortex) and compared expression levels of a subset of glial markers.

Results:: We found a distinct glial expression profile in demented compared to non-demented individuals, which was prior to overt tau deposition. In these preliminary results, the best discrimination between demented compared to non-demented was represented by an increase in activated glial responses. No significant differences in the expression levels of homeostatic microglia were observed.

Conclusions:: Our results suggest that differing glial expression profiles exist in brain regions of demented individuals even prior to overt tau deposition and that these dysfunctional patterns could contribute to diverging cognitive profiles observed in some individuals. Moreover, the predominance of activated glia in clinically relevant brain regions of demented individuals supports early and independent involvement of neuroinflammation in AD pathogenesis before tau accumulation ensues. Lastly, the persistence of a homeostatic glial profile in yet tau-free brain regions could indicate its dependence on tau for later dysfunction and suggest an early window of opportunity for treatment interventions targeting glia-salvaging pathways.
CASE REPORT ABOUT DELAYED ENCEPHALOPATHY AFTER CARBON MONOXIDE POISONING

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**Background and Aims:** We present a case report about Delayed Encephalopathy Carbon Monoxide Poisoning (DEACMP). DEACMP is a group of neuropsychologic disorders that occur after a transient improvement or a symptom-free interval of acute carbon monoxide poisoning. In Mongolia it is diagnosed rarely although during long winter a half of the population burn coal to keep their home warm.

**Methods:** We diagnosed based on course of the disease, clinical symptoms and MRI scans.

**Results:** 51-year-old woman was brought to the ICU by her son with a complaint of she was unable to take care of herself or speak, suddenly. Her co-worker first noticed that 14 days ago the patient did not understand what she was doing at work, with slow reasoning. The disease progressed and after 3 days she could not walk or sit on her own. After 7 days, she became urinary incontinent. When she was admitted to the hospital 14 days after the onset of the disease, the patient was awake but had severe dementia, no obvious paralysis, paresis in the limbs; had urinary incontinence, resting tremor in both hands, and severe ataxia. We initially suspected encephalitis and started treatment with methylprednisolone, but it was ineffective. There was gradual improvement in treatment with complete recovery achieved 90 days after the onset of the disease. We monitored higher mental functions with a Mini-Mental State Examination.

**Conclusions:** DEACMP can be missed because coal is used broadly in Mongolia. So we need accurately to distinguish DEACMP from other diseases that can lead to hyper-progressive dementia.
THE USEFULNESS OF PLASMA NEUROFILAMENT LIGHT IN PATIENTS WITH ALZHEIMER’S DISEASE

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Background and Aims:: A growing body of evidence suggests that the plasma concentration of the neurofilament light (NFL) might be considered another potential biomarker for the clinical use in Alzheimer’s disease (AD).

Methods:: With a single molecule array method (Simoa, Quanterix), plasma NFL levels were measured in 113 subjects with subjective cognitive decline (SCD; n=14), mild cognitive impairment (MCI; n=37), or dementia of Alzheimer type (DAT; n=62). Plasma NFL levels were compared between three diagnostic groups, and its cognitive and clinical correlates were evaluated.

Results:: Plasma NFL levels were correlated with age (r=0.387, p<0.001). NFL levels in plasma were significantly elevated in participants with DAT (65.98±84.96 pg/mL) compared to both groups with SCD (16.90±2.54 pg/mL) and MCI (25.53±10.42 pg/mL), even after adjusting for age (p=0.004). Moreover, plasma NFL levels were different between two groups with amyloid positron emission tomography (PET) (-) (n=17, 25.95±13.25 pg/mL) and PET (+) (n=16, 63.65±81.90 pg/mL, p=0.010). Plasma NFL levels were related with scores of the mini-mental state examination (r= -0.242, p=0.021), clinical dementia rating (CDR) (r=0.291, p=0.005), or CDR-sum of boxes (r=0.276, p=0.008) for all samples.

Conclusions:: This study confirms increased levels of plasma NFL in patients with DAT compared to subjects with MCI and SCD. Plasma NFL levels correlated with global cognitive status and functional state, or dementia severity. Further longitudinal studies are needed to confirm the utility of plasma NFL as a biomarker in the evaluation of AD, as well as in predicting the rate of progression.
DEVELOPMENT OF NOVEL VACCINE TO REDUCE GALECTIN-3 FOR ALZHEIMER'S DISEASE

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Background and Aims:: Alzheimer's disease (AD) is the major cause of dementia and one of the intractable neurodegenerative diseases. There are many reports that neuroinflammation is related to the pathomechanism of AD and microglia have an important role in neuroinflammation of central nervous system. Galectin-3 is a member of the lectin family and has the function related to proinflammatory processes. Recently, some reports said that serum or cerebrospinal fluid galectin-3 levels were elevated in AD patients. In this study, we developed a novel vaccine to reduce galectin-3 and examined the effect of vaccination using inflammation model of mice.

Methods:: We designed a TNF-alpha vaccine using virus-like particle (VLP) and C57BL/6J mice were vaccinated intramuscularly with 10 micrograms three times in 4 weeks (n=5). Two weeks after immunization, serum samples were obtained to measure anti-TNF-alpha antibody titer by ELISA. One week later, we injected 1000 micrograms of lipopolysaccharide (LPS) intraperitoneally and measured serum TNF-alpha and galectin-3 levels of immunized mice by ELISA. As a positive control, 100 micrograms of etanercept was given before LPS administration in the non-vaccinated group.

Results:: All immunized mice showed high titers of anti-TNF-alpha antibody and suppressed the LPS-induced TNF-alpha elevation. Moreover, serum galectin-3 were also suppressed to the vaccinated group. On the other hand, etanercept did not suppress galectin-3 while suppressing TNF-alpha.

Conclusions:: Our results revealed that our novel VLP-TNF-alpha vaccine reduces not only serum TNF-alpha but also serum galectin-3, which suggests our vaccine can be a possible treatment for AD.
DOSE-RESPONSE ASSOCIATION OF THE DURATION AND VOLUME OF PHYSICAL ACTIVITY WITH INCIDENT DEMENTIA: A COSMIC COLLABORATIVE COHORT STUDY

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Background and Aims:: This study aimed to examine the dose-response relationship between the duration and volume of PA and incident dementia.

Methods:: We harmonized longitudinal data from ten community-based cohorts in seven countries. Each PA was recorded and given a specific metabolic equivalent value (MET) for intensity. Total duration of PA (hour) was calculated by summing time spent performing each PA per week. Total volume (MET-hour) of PA was calculated by summing the products of MET and time spent on each PA. Incident dementia was diagnosed after a median of 5.4 years of follow-up. We estimated the multivariate hazard ratio (HR) of each group with the lowest duration or volume as the reference group among five categorized groups by the Cox regression model. Age, sex, educational year, cohort, APOE4, body mass index, smoking, hypertension, diabetes, stroke, and depression were adjusted as confounders.

Results:: A total of 11988 participants were included in our analysis. Significant dose-response associations were observed for the duration and volume of PA and the dementia risk. After adjusted for potential confounders, the corresponding HR ranged from 0.88 (95%CI: 0.67, 1.15), 0.68 (95%CI: 0.52, 0.89), 0.68 (95%CI: 0.51, 0.90), to 0.68 (95%CI: 0.50, 0.93) (p for trend =0.002) with increasing duration, from 0.92 (95%CI: 0.70, 1.22), 0.70 (95%CI: 0.53, 0.93), 0.70 (95%CI: 0.53, 0.92), to 0.63 (95%CI: 0.46, 0.85) (p for trend<0.001) with increasing volume.

Conclusions:: Our study demonstrated significant dose-response relationships between the duration and volume of PA and risk of incident dementia. This evidence could potentially enrich current recommendations for preventing dementia onset.
VESTIBULAR SCHWANNOMAS AND COMMUNICATING HYDROCEPHALUS: A CLINICAL CHALLENGE

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Background and Aims:: Vestibular Schwannomas (VS) can cause both obstructive and communicating hydrocephalus (CH). While the first is due to mass-effect, the pathophysiological mechanisms underlying VS-induced CH are still unclear. The main hypothesis links the proteins secreted by the VS in the cerebrospinal fluid (CSF) to the impaired CSF absorption through arachnoid granulations. Clinical picture and neuroimaging can mimic a normal pressure hydrocephalus (NPH), but the evolution can be much variable, as shown in this case-report.

Methods:: Clinical manifestations, CSF, and neuroimaging findings of a patient with CH and VS are described.

Results:: A 67-year-old man presented with a 2 week history of gait instability and cognitive impairment. Urinary disturbances were present but attributable to prostate hyperplasia. A CT brain scan showed significative ventricular enlargement, then a CSF analysis released extremely high proteins (180 mg/dL). The MRI scan matched the neuroradiological criteria for NPH with the absence of obstructions. Notably, a small VS (<3 cm) was found. In a few days the patient conditions rapidly worsened: he was unable to stand up, then became lethargic and dyspnoeic, finally requiring intensive care assistance for respiratory failure. A ventricular-peritoneal shunt was placed, after which the patient promptly recovered: at one month follow-up the ventricules were markedly reduced and he was independent and well-oriented.

Conclusions:: CH due to VS can easily be mistaken by NPH. Nonetheless, while NPH course is slow, in VS-induced CH the evolution to respiratory failure can be rapid. Therefore, the diagnostic workup is mandatory to rule out this hypothesis and neurosurgical treatment should never be delayed.
RELATION OF MIDDLE CEREBRAL ARTERY FLOW VELOCITY AND RISK OF COGNITIVE DECLINE: A PROSPECTIVE COMMUNITY-BASED STUDY

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Background and Aims:: Hemodynamic parameters measured by the Transcranial Doppler Ultrasound (TCD) are related to cognitive impairment in many cross-sectional studies, but the longitudinal evidence is scarce. This study aimed to verify the association between flow velocity of Middle Cerebral Artery (MCA) and the longitudinal cognitive decline in community dwelling older adults.

Methods:: Participants from the Shanghai Aging Study were administered TCD examination at the baseline. The Peak Systolic Velocity (PSV), Mean Flow Velocity (MFV), and Pulsatility Index (PI) of MCA segments on left middle (LmMCA), left proximal (LpMCA), right middle (RmMCA), and right proximal (RpMCA) were obtained. Mini-mental state examination (MMSE) and cognitive diagnosis were conducted at both baseline and follow-up. The multivariable linear regression model was used to detect the relationship between baseline MCA indexes and the annual rate of decline in MMSE scores.

Results:: One hundred and thirteen participants without dementia were followed up for 6.3 years in average. The mean annual rate of decline in the MMSE score was 0.15 (min to max: -1.0 to 1.2). Lower LpMCA PSV (β = -0.0034, r = -0.231, P = 0.022) and LpMCA MFV (β = -0.0049, r = -0.217, P = 0.031) were associated with higher annual rate of decline in the MMSE score after adjusting for age, gender, education year, APOE ε4, obesity, hypertension, diabetes mellitus, stroke, and coronary heart disease.

Conclusions:: Lower flow velocity of left proximal MCA was related to faster global cognitive decline. Cerebral blood flow velocity may impact the cognitive function.
Background and Aims:: Plasma biomarkers showed a promising value in the disease diagnosis and management of Alzheimer’s disease (AD). This study aimed to investigate the profiles of the biomarkers and the association with cognitive domains in diverse cognitive performance.

Methods:: We recruited 320 individuals with cognitive impairment and 131 cognitively normal participants from a memory clinic and the Shanghai Aging Study. Participants were classified into 6 groups based on their Clinical Dementia Rating (CDR) scores. Each participant was administered the neuropsychological tests assessing the global and domain-specific cognition. Plasma Aβ1-40, Aβ1-42, Aβ1-42/Aβ1-40, total tau (t-tau), neurofilament protein light chain (NfL), and phosphorylated tau at threonine 181 (p-tau181) were quantified using the Single molecule array platform.

Results:: Along with plasma Aβ1-40, Aβ1-42, Aβ1-42/Aβ1-40, t-tau, and NfL, p-tau181 significantly increased across the groups with the incremental CDR scores from NC (CDR = 0) to severe AD (CDR = 3). Compared with other biomarkers, p-tau181 had a stronger correlation with Global cognition (r = -0.536, P < 0.0001), Memory (r = -0.481, P < 0.0001), Attention (r = -0.437, P < 0.0001), Visuospatial function (r = -0.385, P < 0.0001), and Language (r = -0.177, P = 0.0003). Among participants with CDR ≥ 1, higher p-tau181 was correlated with worse Global cognition (r = -0.301, P < 0.001).

Conclusions:: Plasma p-tau181 had a stronger correlation with cognitive domains than other biomarkers, especially in moderate-severe dementia. It could potentially reflect the AD pathology in vivo and may be a promising blood-based biomarker in clinical settings.
EVALUATION OF A SIMPLE VERSUS COMPOSITE PLASMA BIOMARKER MODEL AS SCREENING STRATEGY FOR THE DIAGNOSIS OF COGNITIVE IMPAIRMENT IN CHINESE POPULATION

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Background and Aims: This study aimed to evaluate the diagnostic performance of plasma biomarkers in the Chinese population.

Methods: A total of 428 participants, including 159 AD patients, 148 amnestic mild cognitive impairment (aMCI) subjects and 121 cognitively normal controls, were recruited from a memory clinic cohort and the Shanghai Aging Study. Plasma Aβ 42, Aβ40, Aβ 42/Aβ 40, T-Tau, p-Tau 181 and NFL were quantified using an ultra-sensitive Single-molecule Array (Simoa) platform. The diagnostic models were established based on the plasma biomarkers and clinical characteristics.

Results: A comprehensive diagnostic model, which included all five plasma biomarkers and clinical characteristics, provided the best identification ability with a 95.1% AUC for the AD versus Controls, 78.9% AUC for the aMCI versus Controls and 79.4% AUC for the AD versus aMCI. The simplified diagnostic model that combined only plasma Aβ42 and p-Tau181, along with clinical features, also achieved ideal diagnostic value, with a 93.3% AUC for distinguishing AD from controls, 75.9% AUC for aMCI versus controls, and 77.6% AUC for AD versus aMCI. The comprehensive diagnostic model reached 96.6% AUC for the early-onset AD versus Controls and 95.9% AUC for the late-onset AD versus Controls. The simplified diagnostic model demonstrated 96.6% AUC and 94.0% AUC, respectively.

Conclusions: Our study firstly established AD diagnostic model using plasma biomarkers for Chinese subjects. The simplified diagnostic model could be considered an accessible and practical method for large-scale screening in the clinic and community.
Background and Aims:: Around 2/3 of people with dementia worldwide live in low- and middle-income countries. Alzheimer’s disease (AD) is frequent in Morocco, with an estimated number around 200,000 cases. Diagnosis of dementia in Morocco is challenging and AD is still under-diagnosed.

Methods:: Based on about 30 years’ experience of the Neuropsychological department and more than 22 years of the Memory Clinic, we will present the challenges of AD diagnosis in Morocco and our personal contribution in improving it.

Results:: Dementia in Morocco is still diagnosed at an advanced stage when behavioral disorders appear. This could be explained by more tolerability of cognitive disorders in the elderly, lack of knowledge but also insufficient number of specialists and neuropsychologists. Accessibility to neuro-imaging could also be limiting. Availability of adapted and validated Neuropsychological Tests (NPTs) is challenging. Indeed diagnosis of dementia needs suitable tools but most of NPTs are available in English or other European languages. Adaptation of NPTs in Arabic must consider the linguistic diglossia. In Morocco as in most Arab countries, people use two variants of Arabic, a colloquial Arabic and a standard Arabic. NPTs should use colloquial Arabic for oral parts and standard Arabic for written language. Our team adapted and validated more than 20 NPTs and contributed to the improvement of dementia’s diagnosis.

Conclusions:: To improve diagnosis of AD in Morocco it is necessary to train more specialized health professionals, develop memory clinics and improve accessibility to health structures. This should be coupled with the development of adapted cognitive stimulation therapies and the improvement of home help.
THE COOPERATIVE SUPPRESSION OF LARGE-CONDUCTANCE CALCIUM-ACTIVATED POTASSIUM CHANNEL BY AMYLOID BETA AND AMYLOID PRECURSOR PROTEIN IN CORTICAL NEURONS

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Background and Aims:: We have reported the blockade of large-conductance calcium-activated potassium channel (BK channel) as amyloid-β-induced molecular dysfunction, which we consider leads to disruptive calcium homeostasis and neuron death. The possibility that not just the end product amyloid β but the amyloid precursor protein (APP) per se might be harmful, still remains to be fully studied. This study examined the mode of BK channel blockade mediated by not just amyloid β but also APP.

Methods:: Whole cell recordings were made from the pyramidal neurons in frontal neocortical slices of wild-type (WT) or triple transgenic AD model (3xTg) mice. Spike properties were examined under the intracellular application of recombinant full length APP or various antibodies against APP or Aβ through patch pipette.

Results:: An anti-Aβ-oligomer antibody (11A1), but not anti-monomer-Aβ-antibodies, was effective in recovering BK channel activity in 3xTg neurons. Antibodies against APP were also found effective. In WT neurons, APP as well as Aβ₁–42 suppressed BK channels by itself. In cortical neurons from 3xTg mice that bear Homer1a knockout (4xTg mice), neither anti-APP antibodies nor 11A1, but only the 6E10 antibody that binds both APP and Aβ, rescued the BK channel suppression.

Conclusions:: This study pointed to a different cooperativity of Aβ and APP in WT and 3xTg neurons. Considering that Homer1a expression is activity dependent and 3xTg neurons are hyperexcitable, Homer1a is likely to be expressed sufficiently in 3xTg neurons, thereby alleviating the synergistic suppressive influence of APP and Aβ on BK channel.
DIAGNOSTIC VALUE OF STUDYING NEUROSTEROIDS IN PATIENTS WITH PARKINSON’S DISEASE DEMENTIA

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Background and Aims:: Comparative assessment of the level of dehydroepiandrosterone sulfate (DHEA-S) and cortisol in blood plasma in patient’s with Parkinson's disease dementia (PDD) in the late stages of disease

Methods:: We examined 60 patients with PD, who were divided into two groups : the main group (30 patients) with PDD and the control group (30 patients) PD without dementia. Serum dehydroepiandrosterone sulfate and cortisol values were obtained, taking into account its characteristics depending on the time of day, measured in the early morning between 7:00 and 7:30 on an empty stomach. The state of cognitive functions was assessed using the following scales: Mini Mental State Examination (MMSE), Frontal Assessment Battery (FAB), Montreal Cognitive Assessmet (MoCA).

Results:: Test scales of cognitive impairments characterized by low data on MMSE, FAB and MoCa in patients of the main group. The study of cortisol revealed a tendency to its increase in the blood in patients of the main group, in relation to the control group. The significance of these changes is confirmed by a 2.5-fold increase in blood cortisol in patients with PDD. At the same time, the level of DHEA-S progressively decreased, reaching its minimum value in patients of the main group. The control group in this case occupied a borderline value. Correlation analysis between the studied biomarkers showed their inverse relationship (r = -0.991).

Conclusions:: The diagnostic efficacy of neurosteroids, including the level of dehydroepiandrosterone sulfate and cortisol in the blood serum of patients was established for the early diagnosis of cognitive impairments and monitoring the effectiveness of therapy and identifying a risk group in PD.
COGNITIVE IMPAIRMENT OF ELDERLY IN DALANZADGAD SOUM, UMNUGOVI AIMAG

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Background and Aims:: As of 2015, there were 46.8 million people who had idiocy in the world, and by 2030 this number is expected to increase to 74.7. Cognitive impairment is one of the leading causes of disability in the elderly. This is an irreversible change in the structure and function of the brain, which is a condition for the regulation of family and socio-economic status, reducing the ability to disrupt the daily activities of physical therapy, reducing lifestyle activities.

Methods:: It is a cross-sectional, descriptive and analytical research conducted, and the questionnaire method was used to detect cognitive impairment and the factors that influenced them. From January 10, 2021 to March 10. The questionnaire consists of two general parts. The diagnostic part was the MMSE. An MMSE score below 24 is considered a cognitive change, statistical processing was performed using SPSS-25 software.

Results:: A total of 177 elderly people participated in the survey, with an average age of 69.63, Of these, 67.8% (n = 120) women, 45.0% (n = 54), 32.2% (n = 57) men, and 47.4% (n = 27) had cognitive changes. The study found that 37.8% (n = 67) had mild cognitive impairment and 8.0% (n = 14) had moderate cognitive impairment. Cognitive decline was associated with age (p value = 0.007), marital status (p value = 0.013), education (p value = 0.008), and body mass index (p value = 0.067)

Conclusions:: It was found that cognitive changes among the elderly increase with age, marital status and depend on the level of education.
SPORADIC CREUTZFELDT-JACOB DISEASE PRESENTING WITH CEREBRAL VASOCONSTRICTION

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Background and Aims:: CJD is a rare neurodegenerative disorder promptly leading to a vegetative state caused by abnormal deposits of misfolded prion protein. Due to its tumultuous course and variable clinical characteristics, it can constitute a diagnostic challenge at least in its initial stages. To our knowledge there are no reports to date describing the copresence of vasoconstriction during the course of CJD. By describing this case, we could give impulse to further investigate this fascinating association.

Methods:: A 54-year-old accountant with a 3-year history of recurrent severe headaches followed by variable periods of dizziness and nausea sought our attention lamenting unremitting symptomatology. Her condition was framed as of vascular etiology and underwent extensive workup including transcranial and carotid doppler, lumbar puncture, brain MRI, autoimmune, thrombophilia and tumoral marker search, brain catheter angiography and EEG.

Results:: All were negative save for the catheter angiography evidencing diffuse distal cerebral vasoconstriction, the EEG presenting generalized slowing, and MRI presenting DWI and FLAIR enhanced posterior cortical regions. Her condition steeply worsened in a couple weeks with prominent ataxia, visual field deficits, Balint syndrome and dyscalculia amongst others, until dystonia and myoclonus developed with EEG documenting generalized periodic triphasic delta waves, CSF testing evidenced elevated 14.3.3 levels and positive PrP RT-QuIC. PRNRP polymorphism and prion biochemistry are underway.

Conclusions:: We report for the first time a correlation between probable sporadic CJD and cerebral arterial vasoconstriction, etiologic hypotheses being currently all but presumptive. However, our observation could inspire new studies, hence shedding more light on this terrible yet fascinating disease.
A STUDY OF THE IMPACT OF HYPERTENSION IN COGNITIVE IMPAIRMENT

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Background and Aims:: The previous study of cognitive impairment prevalence and risk factor has shown 39.7% of Mongolian elderly population has cognitive impairment, but the study of cognitive impairment among people with hypertension has not been conducted yet. Objective: To study the impact of hypertension in cognitive impairment.

Methods:: The current study involved 1270 people from the 8 aimags, and 6 districts of Ulaanbaatar city. Mini-mental state examination was used to assess the cognitive function in each subject and cognitive impairment was defined as less than 24 scores. Hypertension was diagnosed if the patient had blood pressure higher than 140/90mmhg during the examination.

Results:: The mean age was 45.6±12.5 and 23.4% of the participants were male. 20.8% of the study population has hypertension and 24.8% has cognitive impairment. The mean MMSE score were statistically significant different between people with hypertension(25.3±4.6) and people without hypertension(26.5±3.5) which means the MMSE score was lower in people with hypertension (p=0.004). The prevalence of cognitive impairment was 33.1%, and 23.4% in people with and without hypertension respectively which was statistically significant (p<0.001). Although the mean MMSE score in people without cognitive impairment was statistically significant different in both groups which was (28.9±0.93) and (27.2±1.93) in people with hypertension and people without hypertension respectively (p=0.042). There was positive correlation between MMSE score and education in both groups, people with hypertension(r=0.370) and people without hypertension(r=0.41)(p<0.001).

Conclusions:: The current study shows that cognitive impairment prevalence is high among people with diabetes(33.1%) without the aging process. This suggests that people with hypertension has a high risk to have vascular(secondary)cognitive impairment.
PREDICTORS OF SURVIVAL IN DEMENTIA WITH LEWY BODIES

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\textbf{Background and Aims::} Dementia with Lewy bodies (DLB), the second most common cause of degenerative dementia, is characterized by a faster progression and earlier mortality compared to Alzheimer’s disease. However, the predictors of survival are still controversial. Our aim was to investigate survival and its determinants in a Tunisian cohort of DLB.

\textbf{Methods::} We conducted a retrospective study over a period of 17 years (2003-2019) in the Department of Neurology of Razi University Hospital, including patients diagnosed with probable or possible DLB according to McKeith criteria. Survival was explored using Kaplan-Meier analysis. Demographic, clinical, neuropsychological features and frequency of Apolipoprotein Epsilon 4 (ApoE\textepsilon{}4) allele were analyzed in the survival analysis.

\textbf{Results::} We included 151 DLB patients (sex ratio=1.2; mean age of onset: 75.3 \pm 7.9 years). First symptoms were mainly non-motor (76.8%). Memory disorders were found in 94.7% and parkinsonism in 87.4%. ApoE\textepsilon{}4 allele was found in 20.5% of the patients. Median survival was 6 years from disease onset. Median survival was significantly shorter in men (6 versus 7 years in women, p=0.005) and in patients with memory impairment at onset (5 versus 9 years, p=0.012). Cognitive fluctuations, familial forms of DLB and ApoE\textepsilon{}4 did not predict the outcome.

\textbf{Conclusions::} Our results support the fact that only gender and inaugural memory disorders help predict survival in DLB patients. Larger prospective studies are needed to better investigate the various survival determinants.
OBSTRUCTIVE SLEEP APNEA IN SPECTRUM OF COGNITIVE DISORDERS ON THE ISLAND OF GUAM

Ramel Carlos
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Background and Aims:: Emerging evidences suggest an association between Obstructive Sleep Apnea (OSA) and various cognitive disorders, including dementia. The degree of OSA has been directly correlated with the severity of cognitive impairment. Vascular disorders are significant comorbidities in these patients. We report the occurrence of OSA in patients with cognitive disorders on the island of Guam and correlate the severity of OSA with the results of the neuropsychological testing (NPT) and neuroimaging studies.

Methods:: A retrospective review and analysis of medical records of patients evaluated in The Neurology Clinic with the diagnosis of OSA in patients with cognitive disorders from July 2016 to July 2020 was conducted.

Results:: There were 762 patients with various cognitive disorders and 17% have been diagnosed with OSA. Among patients with OSA, 45% have severe OSA, 35% have moderate OSA, and 20% have mild OSA. Severe impairment on Global Cognitive Scores was seen in 30% of severe OSA, 40% of moderate OSA and 30% of mild OSA. Evidences of silent stroke were seen in 25% and leukoaraiosis in 35% of patients based on their neuroimaging studies. Vascular diseases including hypertension, diabetes mellitus, hyperlipidemia and cardiac disorders were higher in those patients with severe and moderate OSA compared to those with mild OSA and without OSA.

Conclusions:: OSA is a common comorbidity of patients with various forms of cognitive impairment. The severity of OSA correlated with the degree of impairment on NPT. Silent strokes, various cerebrovascular disorders and leukoaraiosis are more frequent in patients with OSA than those without OSA.
MECHANISM OF AD RISK GENE RIN3 IN AD EARLY PATHOGENESIS.

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Background and Aims:: In AD, about one-third of the risk genes identified by GWAS encode proteins that function predominantly in the endocytic pathways. Among them, the Ras and Rab Interactor 3 (RIN3) is a guanine nucleotide exchange factor (GEF) for the Rab5 small GTPase family and has been implicated to be a risk factor for both late onset AD (LOAD) and sporadic early onset AD (sEOAD). However, how RIN3 is linked to AD pathogenesis is currently undefined.

Methods:: Quantitative PCR and immunoblotting were used to measure mRNA and protein levels. Immunostaining was used to define subcellular localization of RIN3 and to visualize endosomal changes. Recombinant flag-tagged RIN3 protein was purified to define RIN3-interactomes by mass spectrometry. Live imaging of primary neurons was used to examine axonal transport of different proteins.

Results::

A

B

C

D

E
We have shown that RIN3 mRNA level was significantly increased in the hippocampus and cortex of APP/PS1 mouse brain. Basal forebrain cholinergic neurons (BFCNs) cultured from E18 APP/PS1 mouse embryos also showed increased RIN3 expression accompanied by early endosome enlargement. In addition, via its proline rich domain, RIN3 recruited BIN1 and CD2AP, two other AD risk factors, to early endosomes. Overexpression of RIN3 disrupts early endosome trafficking. Together with CD2AP, it increase APP CTFs in PC12 cells. Upregulation of RIN3 or the neuronal isoform of BIN1 increased phosphorylated Tau level. These effects by RIN3 was rescued by a dominant negative Rab5 (Rab5S34N).

**Conclusions:** Our current work has thus provided important insights into the role of RIN3 in regulating endosomal signaling and trafficking in AD early pathogenesis.
Background and Aims:: Ovocystatin has beneficial properties for cognitive function in young rats and might prevent aging-related cognitive impairment in older animals, as well as reduces memory decline in APP/PS1 mice model. Our study aimed at assessing the impact of ovocystatin on microglia activation and neurogenesis.

Methods:: Immunoactivation: Mouse wild type microglia were stimulated with ovocystatin at dose of 100 micrograms/ml. The effect of ovocystatin on nitric oxide production and interleukin 1 beta secretion were determined. Neurogenesis: Primary rat hippocampal neurons of H19-7 cell line was used. The impact of ovocystatin on proliferation, nitric oxide production, and expression of markers of neurogenesis: microtubule-associated protein 2 (MAP2, isoforms A/B and C/D) and Synapsin 1, were determined.

Results:: It was shown that ovocystatin does not stimulate microglial cells to produce inflammatory mediators. Whereas, no toxic effect of ovocystatin (1-100 ug/ml) on H19-7 cells viability, and dose-dependent down-regulation of proliferation were demonstrated. It was also shown that in primary hippocampal neurons of H19-7 cells incubated with ovocystatin (100 micrograms/ml), the expression level of MAP2 C/D (75kDa) - characteristic form of immature neurons is unchanged. However, the increased expression of MAP2 A/B protein (280 kDa) – characteristic for mature neurons was observed after 6 and 24h incubation with ovocystatin. Relatively to MAP2 A/B, increased expression of synapsin 1 was observed.

Conclusions:: The ovocystatin might be a potential activator of molecular mechanisms in primary hippocampal neurons, participating in regulation of neurogenesis. Nevertheless, further studies are needed.
VALIDATION OF AN ALGORITHM BASED ON DATA OF THE HEALTH INFORMATION SYSTEMS (HIS) FOR THE IDENTIFICATION OF DEMENTIA CASES.

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Background and Aims:: The identification of dementia cases with routinely collected health data is a promising method to estimate prevalence and incidence, evaluate temporal trends and improve the interregional comparability. In Italy, a project aimed at the development and validation of an algorithm for the identification of dementia cases has been proposed.

Methods:: The project included four Italian regions (Piedmont, Tuscany, Latium and Campania) and the Italian National Institute of Health. A case of dementia was defined by using pharmaceutical prescriptions, hospital discharge records, residential setting and exemption from treatment co-payment, from 1 January 2012 to 31 December 2016. The validation study involved the comparison of the population identified by HIS through the algorithm with the cases (patients with dementia or Mild Cognitive Impairment-MCI) recruited at the Centers for Cognitive Disorders and Dementias (CDCD), and the controls (subjects without dementia or MCI) recruited at the geriatric centers. Sensitivity, specificity, positive and negative predictive value were calculated.

Results:: Clinical centers identified 1727 cases and 1425 controls. Sensitivity, specificity, positive and negative predictive value of the algorithm were 65.6%, 93.6%, 92.5% and 69.1%, respectively.

Conclusions:: In Italy, despite the presence of several information flows at national and regional level, an integrated information system specifically dedicated to dementias is still not available. Moreover, the results of this project can be used for international comparison with the WHO Global Dementia Observatory on the development of a "core set" of shared indicators on dementia to be routinely collected.
ANTI-DEMENTIA DRUGS: A DESCRIPTIVE STUDY OF PRESCRIPTION PATTERN IN ITALY

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**Background and Aims::** More than one million people in Italy have dementia and nearly 900 thousand people are affected by Mild cognitive impairment (MCI). No effective treatments are yet to be approved and acetylcholinesterase inhibitors (AChEi) and memantine are currently used to reduce cognitive decline related symptoms. Aim of the study is to provide a comprehensive analysis of anti-dementia drugs consumption in Italy between 2014 and 2020 with an analysis of demographic characteristics of the prevalent and incident users. The association between AChEI and memantine or anti-dementia and antipsychotic drugs will be also considered.

**Methods::** Two data sources were used: OsMed database, for the consumption data of medicines and Pharmaceutical Prescriptions database collecting patient level data on medicines.

**Results::** In 2020 the anti-dementia consumption decreased by 3.3% compared to the previous year and increased by 7.7% compared to 2014. The prevalence of use in the population was 0.3% and reaches 2.3% in the over 75 age group, with a higher prevalence in women. Each user has been treated for 242 days, and 15.7% of the users received only one prescription. Acetylcholinesterase inhibitors represent 57% of the total and decreased by 7.5% in respect to 2019, this trend was mainly determined by donepezil (-7.1%) while the memantine consumption increased by 3.0%.

**Conclusions::** This descriptive study should be useful to have an exhaustive overview on appropriateness of anti-dementia drugs in Italy and to support future regulatory decisions to establish eligibility criteria for new therapeutic strategies.
Background and Aims:: In Italy, 1,100,000 people are estimated to have dementia, and almost 900,000 to have MCI. Establishing a relationship between general practitioners (GPs) and Centers for Cognitive Disorders and Dementias (CCDDs) specialists is essential to provide adequate care for patients with dementia (PwD) and their families. The Italian National Dementia Plan defines a specific role for GPs and specialists within diagnostic and therapeutic pathways.

Methods:: Health Search, a research institute of the Italian Society of General Medicine and Primary Care, includes 800 trained GPs, representative of about 40,000 GPs. These 800 GPs have in charge 1,014,016 adults who are representative, for both age and gender, of the Italian population. From 2005 to 2018, the number of contacts by specific cause, by doctor, and per patient per year, and the prevalence of dementia in the primary care setting were collected.

Results:: Results showed that despite an increase in the prevalence of dementia in the primary care setting (from 1.3% in 2005 to 2.9% in 2018), there was a reduction in the number of contacts by specific cause by doctor and per patient per year (from 4.8% in 2005 to 1.0% in 2018).

Conclusions:: Data showed reduction over the years in the level of care of PwD and their families in primary care. This should be further explored across the Italian territory, as it could suggest an increased referral to the CDCDs or specific issues in the level of assistance provided by the National Health System.
ACCURACY OF BIOMARKERS IN PREDICTING CONVERSION TO DEMENTIA IN MCI SUBJECTS: THE STATISTICAL ANALYSIS PLAN OF THE INTERCEPTOR STUDY

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Background and Aims:: Many clinical trials on potentially disease-modifying drugs are focused to mild cognitive impairment (MCI) prodromal-to-Alzheimer's disease. The MCI population actually includes patients with higher risk of progression to AD. Since the new drugs, if effective, will carry both elevated unit costs and not marginal side effects, they should be administered selectively to high-risk subjects. The Italian INTERCEPTOR project, promoted by the Italian Medicine Agency and the Italian Ministry of Health, is a multicenter, interventional, nontherapeutic cohort study in subjects with MCI, with the primary aim of identifying biomarkers that better predict the conversion to AD after 3 years of follow-up.

Methods:: A sample of 500 subjects with MCI was planned to be enrolled. The biomarkers under investigation obtained by the analysis of MMSE, CSF, FDG-PET, FCRST, APOE4, EEG, Volumetric MRI. Multivariate prediction model will provide the predictive performance of each biomarker and combinations. In applying biomarkers, three scenarios are considered: 1) use of cut-offs indicated by experts 2) defining new optimal cut-offs for the specific population 3) use of values in a continuous form in order to evaluate all predictive information. Finally, nomograms will be defined for use in clinical practice.

Results:: Due to COVID-19, the target sample size was not reached. The enrolment was closed on October 31st 2020. Overall 498 patients were screened, 362 recruited into the study and 17 dropped out

Conclusions:: The findings will support the diagnostic path redefinition to identify those patients in the early stage eligible to prescription for disease-modifying medications.
NON-PHARMACOLOGICAL THERAPY OF ALZHEIMER’S DISEASE IN MOROCCO. EXPERIENCE OF THE ALZHEIMER DAY CENTER OF RABAT.

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Background and Aims:: Alzheimer’s disease represent a global public health problem. The effectiveness of non-pharmacological treatment is now well recognized and this therapy is used in developed countries. We present the pilot experience of the day center of Rabat, the first one dedicated to non-pharmacological therapy for AD patients in Morocco.

Methods:: The center of Rabat has been set up in 2017. Its operation is ensured by the Moroccan Alzheimer’s Association. Patients come for half a day, once to three times a week. The center offers cognitive stimulation and speech therapies, physical training, art therapy and occupational activities, as well as guidance and psychological support to the families.

Results:: A total of 80 patients (46 female, 34 male) comes at the center. The mean age is 74.15 (±5.74). The mean MMSE score at the entry is 15.70 (±5.77) for women and 16.74 (±5.75) for men. Patients are divided into 4 cases of amnestic MCI, 19 cases of mild AD and 57 cases of moderate AD. All patients benefit from cognitive stimulation, speech therapy and physical training. Twenty-four of them participate in singing workshops, 18 patients in cooking workshops, 35 in painting and coloring activities and 33 come to dance workshops. The majority of patients positively benefits from this therapy at a cognitive, psychological and behavioral level, specially those with MCI and mild AD.

Conclusions:: Combination of non-pharmacological therapy offer patients the opportunity to maintain cognitive and behavioral functioning, preserve social relations and reduce burden of caregivers. This pilot experience in Morocco should be multiplied in developing countries.
MORTALITY ASSOCIATED WITH ANTIPSYCHOTIC MEDICATIONS IN OLDER PATIENTS WITH DEMENTIA: A POPULATION-BASED STUDY IN THE LAZIO REGION, ITALY

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Background and Aims:: Antipsychotic drugs (AP) can be effective in reducing behavioral and psychological symptoms of dementia but they are associated to a wide range of serious adverse events. This study aimed to evaluate all-cause mortality at 30 and 180 days, and 1 year after the first prescription with an AP, and the risk of death associated with the use of typical versus atypical AP medications.

Methods:: A population-based cohort study was conducted in the Lazio region using data from administrative health databases. Individuals with dementia aged 65 years and over at 31/12/2016 were identified. Only new users with a first claim of AP between 01/01/2017 and 30/11/2019 were considered. For each new user, one age- and gender-matched non-user or typical vs atypical AP user was randomly selected. Adjusted estimates were obtained by using propensity score matching.

Results:: We identified an overall population of 34,625 patients (67% females). Three different cohorts were enrolled including 6047, 5529 and 4730 new users of AP, respectively in the 30-day, 180-day and 1-year mortality cohort. An excess of mortality at 30 days and 1 year since the first prescription of an AP was observed (HR: 1.30, 95%CI 1.01-1.68 and HR: 1.60, 95%CI 1.39-1.69, respectively). Typical APs users showed a significantly higher risk of death within 1 year than atypical APs users (HR: 1.30, 95%CI 1.01-1.62).

Conclusions:: AP use is associated with an increased short- and long-term mortality risk in elderly with dementia. The prescription of AP, especially typical AP, should be carefully evaluated and stringently monitored overtime.
BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS IN DEMENTIA, OFTEN REVERSIBLE CONDITIONS

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Background and Aims:: In the later stages of dementia some people with develops what's known as behavioural and psychological symptoms of dementia, BSPD. Symptoms of BPSD can include increased agitation, aggression, delusions, hallucinations, sleep disturbance and night-time waking. Behaviour changes could be caused by brain-related issues or from changes to someone's environment, health or medication.

Methods:: Dementia is an umbrella term used to describe a group of symptoms that affect brains work. Many conditions, such as stroke, depression, infections, as well as normal ageing, can cause dementia-like symptoms. We describe 120 patients than have been admitted in the emergency setting because of acute symptoms. We examined the patients to see if they have any infection, pain constipation, depression or side-effects of their medicine that could be contributing to or causing the behavior.s change.

Results:: The mean age was 81,68 women and 52 men. Hypertension was present in 96 and vascular changes in the brain were found in the neuroimaging. 78 patients had reversible symptoms of dementia due to such conditions: urinary infection, hydration, costipation, fever and Covid infection.

Conclusions:: Dementia is always changing and unique for each person. Everyday life can be a stressful ordeal for a person with a dementia-related disorder. As the disease progresses, behaviors changes can occur. The pandemic worsened such situation. It is important in the acute setting to rule out any concomitant illness that can cause or worsen behavioral and psychological symptoms in dementia.
CLINICAL CHARACTERISTICS AND DEMOGRAPHICS OF PATIENTS WITH DEMENTIA TREATED AT THE NPZR

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Background and Aims:: Dementia is considered as an important public health issue with high costs for the treatment of the patients. Previous studies demonstrate that low education and the age of people were significantly associated with a greater risk for dementia (Sharp & Gatz, 2011 and Gao, et al., 1998). Therefore, this study aims to analyze the relationship between sociodemographic parameters as well as the prevalence of depression of patients with dementia treated at the NPZR.

Methods:: A total of 283 patients (33.1 %, n=98 male and 62.5%, n=185 female) diagnosed with dementia between 2015 and 2021 were recruited in this research from our patient files of the NPZR. The participants were tested with the DemTect.

Results:: As expected, the prevalence of dementia increases with age. 47.3 % of patients with dementia (n=140) were over 85 years old. While 68.2% of patients with dementia were German citizens, the percentage of patients with Turkish immigrant background was 19.9 %. 57.3 % patients with dementia had severe depression. In particular, there is a significant relationship between gender and severe depression. Female patients with dementia had more severe depression (p<0.005). Furthermore, low education level and current employment status were significantly associated with dementia. The prevalence of dementia was higher among the participants with a primary school degree (p=0.002) and retired patients (p=0.001).

Conclusions:: Depression is a significant factor for dementia, particularly among female participants. Prevalence of dementia was higher among participants with over 85 years old, low education level as well as retired participants.
FREQUENCY OF DEMENTIA AMONG PATIENTS ADMITTED TO BENGHAZI MEDICAL CENTER OVER A SIX MONTHS PERIOD IN 2017

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Background and Aims:: Background: With the rising age of the general population in developing countries it is expected that age-related hereditary neurodegenerative disorders such as dementia will become important health issues. In many elderly patients cognitive decline is multifactorial and exists with other comorbidities. There are currently few data on dementia in Libya. Aims: To determine the size and thereby the impact of dementia in our hospital patient admissions.

Methods:: A retrospective study using a prepared study proforma of a sample of the case notes of 2000 patients admitted consecutively over a six month period to the Medical Department, and of whom 437 were of the Neurological Unit at Benghazi Medical Center in 2017, from 1st July 2017 to 31st December 2017.

Results:: Frequency of Dementia in Medical Admissions: 7.5/1000 Dementia was identified in 437 admissions to the Neurological Unit. Frequency of Dementia in Neurological Admissions: 34/1000 (3.4%). Alzheimer’s disease was identified in 9 patients 4.5/1000 of medical patients, and 20.6 /1000 (2.1%) of neurological admissions. Alzheimer’s disease age Range 65-95 Gender ratio: 1.25: 1 Dementia was documented in 15 patients of whom 5 had coexisting vascular pathology, 4 epilepsy, and one Parkinson’s disease.

Conclusions:: Dementia is a recognized cause for hospital admission. We found a rate just short of that of western countries. We may have underestimated the size of the problem. Prospective multicentre studies may give more accurate data regarding this condition in Libya. They would determine whether we had similar rates to others or that the condition is rare in Libya.
INTRANASAL DELIVERY OF INSULIN FOR THE RESTORATION OF MEMORY SIGNALING IN ALZHEIMER DISEASE

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Background and Aims:: Alzheimer's disease (AD), is progressive, degenerative brain disease characterized by marked atrophy of cerebral cortex and loss of cortical and sub-cortical neurons. Weakening of insulin receptor signaling is involved in ageing-related brain degeneration like AD. Objective of this study is to develop delivery-system to overcome BBB by employing novel, non-invasive approach via nasal route i.e. delivery of antibody appended Insulin encapsulated carrier, PEGylated nanoparticle coated with chitosan to facilitate nasal absorption for efficient transfer to brain.

Methods:: PEGylated-PLGA-nanoparticles were prepared by modified Double Emulsification method and coated with chitosan. Characterization was done by FTIR and NMR. In-vivo study comprised biodistribution in various organs and fluorescence microscopy, estimation of Anti-Aβ antibody, PET- Imaging of Brain, Hemolytic Toxicity studies, Histopathology of Nasal Mucosa and Brain with Blood Glucose Level Monitoring.

Results:: Degree of hemolysis showed PEGylated(PEG-NP’s) and chitosan-coated nanoparticles(cPEG-NP’s) were less toxic. Blood glucose monitoring indicates reduction in blood glucose level in cPEG-NP’s. Biodistribution assessment suggests nanoparticles showed maximum availability at olfactory bulb entrance. Uptake study shows intense fluorescence in brain revealing higher uptake of nanoparticles. These studies highlight possible biological significance of cPEG-NP’s for delivery to brain.

Conclusions:: Results from various studies suggest nanoparticles are effective delivery system for targeted delivery of insulin in brain for an extended period. Coating with chitosan elicits associated benefits in addition to prolonging uptake via intranasal route. This project may provide sound platform towards employment of this modified nanoparticulate carrier for brain delivery of proteins and peptides towards intranasal delivery of insulin for restoration of memory signaling in Alzheimer patients.
PRESENT CLINICAL PRESENTATIONS OF SYPHILITIC DEMENTIA: STUDY OF 9 OBSERVATIONS AT DEPARTMENT OF NEUROLOGY, ACADEMIC HOSPITAL, UNIVERSITY OF CONAKRY

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Background and Aims:: the goal of a reassessment of this pathology from a clinical and paraclinical point of view.

Methods:: We conducted a retrospective study of 298 patients hospitalized for dementia syndrome between 2010 and 2019 in the Neurology and Psychiatry Departments of the Academic Hospital, University of Conakry. Syphilitic etiology was selected for 9 patients.

Results:: L’étiologie syphilitique a été conservée chez 9 patients âgés de 55 à 76 ans (3 femmes et 6 hommes). Un tableau clinique dominé par des troubles de la mémoire avec une diminution de l'idéation, des troubles de la personnalité et du comportement et un syndrome pseudo dépressif a été noté chez les patients. Ce tableau était augmenté par la présence de signes neurologiques: signe d'Argyl-Robertson (5 cas), tremblement vermiculaire de la région labio-linguale (3 cas), troubles du sphincter (3 cas) et faciès pseudo-parkinsonien (6 cas). Le diagnostic était basé sur la positivité des réactions sérologiques (VDRL-TPHA) dans le sang et le liquide cérébro-rachidien, la présence d'une hypercellularité principalement lymphocytaire et d'une hyperprotéinorachie.

Conclusions:: These neurological syndromes, expression of a cerebral syphilitic attack, are the result of still poorly managed treatment of primary and secondary syphilis in our country.
QUALITY OF LIFE COMPARED IN MILD COGNITIVE IMPAIRMENT, ALZHEIMER’S, FRONTOTEMPORAL, LEWY BODY, AND VASCULAR DEMENTIA.

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Background and Aims: Quality of life (QOL) is of great importance in dementia. We examined QOL across types of dementia in patients presenting to a rural and remote memory clinic (RRMC).

Methods: This analysis included 343 RRMC patients seen consecutively between 2004 and 2016. Patients were diagnosed with mild cognitive impairment (MCI, n=74), frontotemporal dementia (FTD, n=42), Alzheimer’s disease (AD, n=187), vascular dementia (VD, n=22), or Lewy Body dementia (DLB, n=18). Patients and caregivers completed questionnaires at their visit. Data collection included patient-rated patient QOL (QOL-PT), caregiver-rated patient QOL (QOL-CG), MMSE score, age, and other patient demographics. Statistical analysis assessed patient variables and differences in QOL across types of dementia using one-way ANOVA, χ² tests, and t-tests.

Results: QOL-PT did not differ by diagnosis, whereas QOL-CG did. QOL-CG was significantly higher in MCI (34.6±7.1) compared to FTD (30.9±5.2) and AD (31.7±5.9). QOL-PT and QOL-CG differed in certain dementia subtypes. QOL-PT was significantly higher than QOL-CG in MCI (QOL-PT=37.3±5.0, QOL-CG=35.3±7.3), FTD (QOL-PT=37.2±6.1, QOL-CG=31.7±5.5), and AD (QOL-PT=37.0±9.7, QOL-CG=32.1±5.9).

Conclusions: We found that QOL-PT does not differ across dementia subtypes, QOL-CG is higher in MCI compared to FTD and AD, and patients rate their own QOL higher than their caregivers do in MCI, FTD, and AD.
SUPERO-TEMPORAL RETINAL AMYLOID COUNT PREDICTS HIPPOCAMPAL VOLUME, VERBAL MEMORY AND COGNITIVE-RELATED QUALITY OF LIFE

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Background and Aims:: As retinal amyloid deposition correlate with and even precede brain amyloidosis, retinal imaging may become a non-invasive and non-ionizing biomarker for Alzheimer’s disease. Retinal autofluorescence using a specific amyloid-binding fluorophore curcumin and laser ophthalmoscopy is an emerging methodology for retinal amyloid quantification. In this study, we aimed to evaluate the relationship between the retinal amyloid counts (RAC) in the supero-temporal quadrant and brain volumes, and cognitive performance.

Methods:: 29 patients with cognitive impairment underwent curcumin-enhanced retinal fluorescence imaging, 3-Tesla brain MRI and standard neuropsychometric testing. RAC was calculated in the supero-temporal quadrant. Automated NeuroQuant software was used for volumetric brain analysis. Logistic regression analyses were performed to appraise the association between RAC, brain volumes and various cognitive domains’ Z-scores.

Results:: Supero-temporal RAC was significantly higher in patients with lower MOCA scores (p<0.05). The total RAC significantly correlated with hippocampal volume (r = -0.39, P=0.04), but not with total brain volume (P =0.08). Total amyloid significantly predicted SF-36-Mental Component Score (Beta -0.004 (SE 0.002), P=0.046). On subregional analysis, proximal mid-periphery RAC significantly predicted verbal memory measures, CVLT-II Long Delay (Beta -0.009 (SE 0.003), P=0.027) and WMS-IV LM-II (Beta -0.007 (SE 0.003), P=0.028). Distal mid-periphery RAC predicted non-verbal memory, RCFT delayed recall (Beta -0.01 (SE 0.005), P=0.04) and SF-36-MCS (Beta -0.014 (SE 0.004), P=0.004).

Conclusions:: Supero-temporal quadrant RAC correlates with hippocampal volume and predicts cognitive related-psychological functioning. Proximal mid-periphery amyloid predicts verbal memory. Future larger studies should evaluate the utility of curcumin-enhanced retinal imaging in monitoring brain amyloidopathy.
COMPUTATIONAL MODEL OF THE FLANKER TASK IN PATHOLOGICAL AGING

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Background and Aims:: Attention control problems are typical of the aging brain. The aim of the study was to assess the functioning of attention control in mild cognitive impairment (MCI) via the application of a computational model of flanker task performance.

Methods:: 39 patients diagnosed with MCI took part in the study and 41 healthy older adults (mean age = 57.32, 19 female). They performed the arrows flanker task with two flankers on each side. The shrinking spotlight model (SSP) model was fit using the flankr package in R.

Results:: The MCI patients performed worse on RT in accuracy on average and, specifically, in the incongruent flankers condition. Comparing the SSP parameters between groups revealed significant differences in the $\text{sd}_\alpha$ parameter which reflects the dispersion of attention distribution over the stimuli with wider attention dispersion in the pathological case.

Conclusions:: It is concluded that MCI characterized by more dispersed attention and more perceptual distractability as a consequence. Using computational models of cognitive tasks used in neuropsychological and neurological research in pathological aging.
Background and Aims:: Frailty, a clinical syndrome characterized by vulnerability to stressors resulting from multisystemic loss of physiological reserve, predicts future cognitive decline. However, little is known about whether frailty is associated with risk for dementia. The study aim was to determine the cross-sectional association of frailty with dementia risk in older Veterans.

Methods:: Community-dwelling Veterans ≥50 years completed a mailed socio-demographic questionnaire and Self-Administered Gerocognitive Examination (SAGE), July 2019-May 2020. The information was complemented with electronic health record data. We calculated the CAIDE score, a validated tool predicting dementia (≥6 points=high risk 20 years later) and the 31-item VA frailty index (VA-FI) data (frail>.20, non-frail≤.20). After adjusting for socio-demographic characteristics, smoking, alcohol/substance abuse, obstructive sleep apnea and anticholinergic use, odds ratio (OR) and 95% confidence intervals (CI) were calculated using binomial logistic regression to assess the association between frailty and dementia risk (CAIDE≥6 points and MCI).

Results:: The survey response rate was 19.75% (1,073 of 5,432). Participants mean age was 68.38(SD=8.49) years, 57.50% (n=617) Caucasian, 69.34% (n=744) non-Hispanic, 95.81% (n=1,028) male, and 36.72%(n=394) frail. 11.84%(n=127) screened positive for MCI and 15.38% (n=165) for dementia. 689 (75.88%) veterans were at high risk for dementia of whom 426 (61.83%) were non-frail and 263 (38.17%) were frail. Frailty was associated with higher risk for dementia, adjusted OR:1.45 (95%CI:1.016-2.070), p=.041.

Conclusions:: Frailty was cross-sectionally associated with higher risk for dementia in older Veterans. Early identification of patients with frailty can help in the implementation of interventions aimed at preventing or delaying dementia.
MEDIAL TEMPORAL LOBE ATROPHY, BUT NOT CSF BIOMARKERS, CORRELATES WITH COGNITIVE IMPAIRMENT IN ALZHEIMER’S DISEASE

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Background and Aims:: The reliability of cerebrospinal fluid (CSF) biomarkers in reflecting the rate of cognitive decline in patients with Alzheimer’s Disease (AD) is still controversial (Williams et al., 2011). Our study aimed to correlate CSF biomarkers, MTL atrophy, cerebral white matter disease, and cognitive performance in patients diagnosed with AD.

Methods:: We retrospectively analysed the data of 24 patients meeting the IWG-2 criteria for typical AD. We tested for correlations between CSF levels of biomarkers for AD (β1-42, t-Tau, p-Tau and combined ratios) and measures of medial temporal lobe atrophy (MTLA), white matter disease, and cognitive impairment (neuropsychological tests for memory, attention, executive functions, and visuo-constructive abilities).

Results:: No statistically significant correlations between CFS biomarkers and any cognitive measure was detected; MTLA correlated negatively with episodic memory tests; cerebral white matter disease correlated negatively with attention and executive functions measures. No statistically significant correlation between CFS biomarkers and the MTLA was detected.

Conclusions:: Our results confirm the widely accepted correlation between medial temporal lobe atrophy and episodic memory impairment and between cerebral white matter disease and attention-executive dysfunction. Conversely, no statistically significant correlation between CFS biomarkers and cognitive measures were detected. Our results show that CFS biomarkers, although effective in providing early disease detection, may not be reliable as indicators of disease severity.
INTEREST OF CEREBROSPINAL FLUID BIOMARKERS FOR PRODROMAL ALZHEIMER'S DISEASE DIAGNOSIS: ABOUT 4 CASES

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Background and Aims:: Alzheimer’s disease (AD) is the main cause of dementias. It is characterized neuropathologically by senile plaques, mainly made up of beta-amyloid peptide aggregates (especially in its AB42 form) and neurofibrillary degeneration (DNF), the main constituent of which is the Tau protein, in its hyperphosphorylated form. The prodromal phase of AD in its typical form is manifested by impairment of episodic memory, without major repercussions on autonomy. Biologically, the accumulation of the Tau protein precedes the first symptoms from 10 to 15 years. Biomarkers of AD in the cerebrospinal fluid (CSF) accessible during the patient's lifetime can testify to Alzheimer's disease. Indeed, the current stake of the diagnosis of AD, is at the pre-dementia stage, in the perspective of the development of drugs likely to act on the etiology of the disease.

Methods:: All the patients underwent a neuropsychological evaluation, cerebral imaging, a biological assessment. CSF biomarkers were carried out in all cases with assay for the AB1-42 protein, the total Tau protein (T-Tau), the phosho Tau (P -Tau) as well as the calculation of the 'IAT1 (INNOTEST amyloid tau index) and AB42 / P-Tau, Tau / AB42 and P-Tau / AB42 ratios.

Results:: On the basis of the diagnostic criteria of the NIA-AA "National Institute of Aging-Alzheimer's Association", was retained in the 4 cases: - MCI due to AD with an intermediate probability: 1 case. - MCI due at AD with a high probability: 3 cases.

Conclusions:: We highlights the advantages of CSF biomarkers for predicting the risk of progression from MCI to AD.
THE TIRNA&TREF EXPRESSION IN APP/PS1 TRANSGENIC MICE AND THE CHANGE OF RELATED PROTEINS EXPRESSION

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Background and Aims:: Alzheimers’ disease (AD) was the major reason of dementia worldwide. Recently some researchers focused their attention on transcriptomics, such as the non-coding RNA, which include the tRNA derived fragments (tiRNA&tRF). tiRNA&tRF was a fragment produced by the tRNA split at specific sites. The expression of tiRNA&tRFs in AD has not been fully illustrated.

Methods:: We screened the differentially expressed tiRNA&tRF fragments with next sequencing technology between APP/PS1 mice (Alzheimer’s disease model) and the healthy control WT mice, then observed the possible biological functions regulated by tiRNA&tRFs in APP/PS1 mice.

Results:: A total of 27 tiRNA&tRFs were found differentially expressed between APP/PS1 mice-14 up-regulated and 13 down-regulated, among which the tRF-Thr-CGT-003 and tRF-Leu-CAA-004 were found to regulate the calcium regulation related proteins (the voltage gated calcium channel γ2 subunit and the RYR1 endoplasmic reticulum calcium released protein) and the retinol metabolism related proteins (the retinoic acid metabolic enzymes CYP2S1, CYP2C68, CYP2S1).

Conclusions:: In general, we had found the expression change of some tiRNA&tRFs in APP/PS1 mice, which may be closely connected with the amyloid β production, but whether the tiRNA&tRFs expression change was a direct cause of Aβ production or just a secondary change of Aβ production need further research. Besides, we found the tRFs took part in the voltage gated calcium channel γ2 subunit expression and regulation, influencing the neuron calcium hemostasis. Moreover, we also found the tRF also participated the regulation of retinol metabolism. The present study provides novel insights for future investigations to explore the AD related mechanisms.
DIGITAL DEVICE USAGE AND SUBJECTIVE MEMORY COMPLAINTS DURING COVID-19 PANDEMIC AMONG YOUNG ADULTS

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Background and Aims:: Digital devices have potential mental health impact impairing cognitive abilities. Digital dementia refers to memory impairment related to use of digital devices. The use of digital gadgets has exponentially increased during pandemic times; this study was planned to find correlation between digital devices and subjective memory complaints.

Methods:: Structured questionnaire was shared online with study participants followed by cognitive assessment through Montreal Cognitive Assessment (MoCA), performed online. The responses were kept anonymous and their consent was taken digitally. A total of 50 subjects were chosen for online assessment of their cognition level via MoCA.

Results:: There were a total of 208 responses collected, distributed in a ratio of (M:F=107:101). The mean age of participants was (25.92±6.35 years). All participants were using smart phones and 204 participants (98.1%) were surfing internets using a mobile phone. Mean duration of mobile phone usage was 359.8±219 minutes per day. Mean duration of internet usage was 327±233 minutes per day. A total of 47.1% of participants felt ‘addiction’ to the internet and 52.4% participants agreed forgetfulness in their daily routine. A total of 21.4% participants related their forgetfulness to usage of digital devices. A total of 50 subjects were assessed online through MOCA with scores 26.14±2.55 (max score=30) with 28 (56%) participants had MoCA scores ≤26. Out of these 28, 18 (64%) subjects felt they were forgetful.

Conclusions:: Widespread digital devices usage during pandemic is probably affecting cognition levels among young adults as shown by significant number of participants who agreed subjective memory complaints in the current study.
MECHANISMS OF DEVELOPMENT OF COGNITIVE IMPAIRMENTS AFTER OCCLUSION OF CAROTID ARTERIES

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Background and Aims:: The study was aimed at determining the role of vascular endothelial dysfunction in induction of molecular and cellular mechanisms of the development of cognitive impairments after occlusion of common carotid arteries.

Methods:: The experiments were carried out on Wistar rats divided into groups: sham; rats with cerebral ischaemia-reperfusion. The model of cerebral ischaemia-reperfusion was reproduced by occlusion of common carotid arteries for 5 min. The degree of endothelial dysfunction was assessed by determining the amount of circulating endotheliocytes and concentration of nitrogen oxide in plasma. In the brain, we measured the content of malonic dialdehyde, the activity of superoxide dismutase and catalase. Pathomorphological studies of cerebral structures were carried out by means of light microscopy. Cognitive functions in rats were assessed by means of conditioned reaction of passive avoidance and the object recognition test.

Results:: Occlusion of carotid arteries in rats induced an increase in the level of circulating endotheliocytes and a decrease nitrogen oxide in plasma; the content of malonic dialdehyde in the brain increased 2.6-fold, the activity of superoxide dismutase and catalase decreased 5.9-fold and 2.8-fold, respectively. The findings of morphological examination registered signs of vasoconstrictive reactions, damaged neurons in the neocortex and hippocampus. It was determined that occlusion of carotid arteries in rats resulted in memory decline.

Conclusions:: Occlusion of carotid arteries in rats becomes a cause of endothelial dysfunction, damage of neurons in the neocortex, hippocampus and cognitive impairments. Damaging factors of the brain are intensification of oxidative processes and a decrease in the level of antioxidant defence.

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AN UNUSUAL PRESENTATION OF MEMORY LOSS

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Background and Aims:: Multiple system atrophy (MSA) is a neuro-degenerative disease, pathologically characterized by α-synuclein (αSyn)-immunopositive glial cytoplasmic inclusions (GCI). Comparing to other synucleinopathies such as Parkinson’s disease (PD) or Dementia with Lewy body (DLB), MSA has not been characterized by dementia. However, recent studies reported that various types of cognitive impairments could be presented in MSA.1 We report a case of MSA with severe cognitive impairment that proceeded 6 years before cerebellar dysfunctions of MSA.

Methods:: 65 year old female presented to neurology op with complaints of giddiness with frequent falls, difficulty in walking, memory impairment. Known case of hypertension and diabetes on treatment. Initially patient diagnosed as dementia on treatment now they are not taking medication. On examination, conscious oriented walking with support, extraocular movements decreased.

Results:: MRI imaging revealed diffuse cerebellar atrophy, mammillary body atrophy with humming bird sign in midbrain, periventricular and white matter changes. Other investigation within normal limits.

Conclusions:: This patient had shown rapid progressions of memory impairment, behavioral changes and impairment in executive functions, and been diagnosed with dementia initially. Thereafter, cerebellar ataxia with dysautonomia and had occurred, and finally he was diagnosed with MSA-C. MSA is a neurodegenerative disease, which usually occurs sporadically in adults, older than 30 years. Typically it is presented with parkinsonism, cerebellar ataxia, dysautonomia and pyramidal dysfunction. Pathologically, neuronal cell loss, gliosis and αSyn-immunopositive GCI are observed in structures of striato-nigral pathway and olivo-ponto-cerebellar pathway. In this case MSA with dementia is rare. This case may suggest that the clinical diagnosis of MSA could not be excluded by the presence of dementia.
CAN SPORADIC CREUTZFELD-JAKOB DISEASE BE STRESS-TRIGGERED? – A CASE REPORT

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Background and Aims:: Affecting many cerebral areas simultaneously, Creutzfeldt-Jakob disease (CJD) mimics several neurological and psychiatric conditions, especially in the earlier phases of the disease, thus representing a challenging diagnosis. Scarce scientific literature based upon laboratory and retrospective cohort studies, suggests the existence of a stress hypothesis explaining an eventual association between stress and CJD expression and progression.

Methods:: A case of a 62-year-old patient, diagnosed with CJD, with symptoms onset after a family conflict is presented.

Results:: A 62-year-old female patient was admitted at the emergency department due to a progressive neuropsychiatric disorder, characterized by abnormal behavior and gait apraxia. Symptoms had been first noticed by relatives 8 weeks earlier after an intense family conflict. A brain MRI did not reveal significant findings, supporting an initial diagnosis of depressive catatonia. The patient was transferred to a psychiatric ward, where she rapidly evolved to refractory convulsive status epilepticus and later coma. An EEG with generalized periodic triphasic complexes, a CSF 14-3-3 protein level superior to 80000AU/mL and a new MRI with cortical ribboning supported a diagnosis of CJD, with progression to death in 11 weeks after symptoms onset.

Conclusions:: Despite strict temporal relationship between symptoms onset and a stressful event, causality cannot be established. One may argue both events are only coincidental or that conflict itself might have been the result of the disease’s behavioral presentation. Further studies are needed to clarify the relationship between stress and CJD.
THE FUNCTIONAL ROLE OF CEREBELLUM IN VISUAL HALLUCINATIONS

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\textbf{Background and Aims::} The role of the cerebellum in behavioral symptoms of dementia is still largely unknown. We explore cerebellar structural and metabolic correlates of visual hallucination in dementia-with-Lewy bodies (DLB)-related VH

\textbf{Methods::} Thirty-five subjects with a diagnosis of probable DLB (21 without-VH and 14 with-VH) matched for age and sex (69.4 ± 6.93 years and 72.8 ± 6.18 years, respectively) were studied with brain FDG-PET/MR integrated scan 3T. We used SUIT algorithm for segmentation and anatomical parcellation to extract cerebellar volumes. Partial volume correction was performed with an inhouse algorithm based on the Symmetric Geometric Transfer Matrix of PET data. Brainstem was used as reference region to obtain regional cerebellar standard uptake value ratios (SUVr). Analysis of variance controlled for eTIV was done for the comparison of each anatomical volume of the cerebellum and corresponding metabolic region, adding age and sex as covariate

\textbf{Results::} Hallucinators showed lower FDG-uptake values in the right and left lobule VI and IX and Crus I, in the left lobule VIIb and VIIIa (p<0.05). Greater severity of VH correlated with lower metabolism in the left and right lobule IX (\(\rho=-0.52\) and \(\rho=-0.54\) respectively, pcorr<0.005). As for the analysis of atrophy we found in hallucinators atrophy of right Crus I, lobule IX and X (puncorr<0.05) but the results
Conclusions:: Cerebellar lobule IX belongs to functional dorsal attention and default mode networks. This results highlight the functional contribution of cerebellum in VH as part of functional networks of goal oriented attention and default mode.
Background and Aims: A proportion of patients with neurodegenerative dementia (DLB, FTD or AD) present with treatment-resistant affective disorder or psychosis and diagnosis is a challenge. We study: the prevalence and type of neurodegenerative diseases among a sample of patients presenting with late-onset depression or psychosis followed longitudinally for two years and the cognitive differences between neurodegenerative diseases and PDD.

Methods: 63-subjects with a first time late-onset-psychiatric episode were prospectively enrolled at Neurology-Clinic-of-Padova-Hospital and Casa-di-Cura-Parco-dei-Tigli. All patients were neuropsychologically and clinically tested. An epidemiological analysis was performed evaluating the prevalence of psychiatric diagnosis at admission and the diagnosis after clinical evaluations/follow-up. We conduct a data driven analysis with principal component. We validate the results of the analysis with a subsample of patients that receive a biological diagnostic markers.

Results: Patients enrolled obtained the following psychiatric diagnoses: 32/56 major depression, 12/56 bipolar-disorder, 8/56 psychosis, 4/56 obsessive-compulsive disorders. About 50% of patients with major depression had cognitive deficits, about 15% of BD, about 100% of psychosis and 75% of OCD (CHI2=14.35, p<0.01). Overall, about 50% of patients have a cognitive decline. The multivariate analysis showed that psychotic patients are had worse cognitive performances respect to patients with affective disorders. Considering the final diagnosis, multivariate analysis showed different cognitive profile between AD/DLB patients and FTD/PDD.
Conclusions:: A late-onset psychiatric symptom masks a diagnosis at follow-up of neurodegenerative disease in about 50% of cases. We encourage a multidisciplinary evaluation in the assessment of late-onset psychiatric manifestations and suggest some clinical and cognitive red flags of help in the differential diagnosis.
Background and Aims:: Chronic cerebrovascular disease is progressive pathology with gradual development of cognitive disorders. In the treatment of cognitive disturbances, drugs with comprehensive antioxidant, angioprotective, neuroprotective and neurotrophic action are usually used. The present study is aimed at evaluating the effect of the multicomponent herbal extract on cognition disturbance after unilateral occlusion of common carotid artery in rats.

Methods:: The Wistar rats were divided into three groups: sham, ischemia and herbal extract. The model of cerebral ischaemia was induced by occlusion of the left common carotid artery. Group 3 received extract 100 mg/kg p.o. for 4 weeks after ischemia. The extract was obtained from of Crataegus sanguine Pall., Hippophae rhamnoides L., Rosa canina L., Scutellaria baicalensis Georgi, et other. Effects of extract on the spatial memory in rats were examined, using the 8-arm radial maze. Error of reference and working memory were used as indices of spatial memory deficits.

Results:: The rats subjected to occlusion of the left common carotid artery exhibited a significantly more number of working errors and reference errors in 8-radial maze test compared with sham (p≤0.05). The course introduction of extract limited the development of cognitive disorders. The 4-weeks regimen with extract significantly improved spatial memory impairments induced by ischemia in the 8-arm radial maze test (working and reference errors, p≤0.05).

Conclusions:: The use of the extract limits the development of cognitive impairments in rats with cerebral ischemia due to the multitarget effect of herbs combinations. Effective nutraceutical prophylaxis can be explored as a approach to reduce the cognitive disturbances.

This research was funded by the Ministry of Education and Science of Russia, grant number - 121030100227-7.
Background and Aims:: Post-stroke dementia includes all dementias that appear following a cerebral infarction within a period of 3 months to 3 years. They are mainly represented by Alzheimer's dementia, whose preclinical phase is shortened by stroke. Vascular dementia represents 19 to 60% of post-stroke dementias depending on the diagnostic criteria used in the studies.

Methods:: We report the case of a 42-year-old female patient, with a history of arterial hypertension, hypercholesterolemia and ischemic stroke at the age of 36, manifested by a left hemiparesis with facial involvement, who presented cognitive and psychocomportemental disorders with a repercussion on the activities of daily life. The neurological examination revealed a left hemiparesis with brachiofacial predominance. The brain MRI revealed areas of hyperintensity on T2 Flair, T2 and T2* gradient echo, reaching the supratentorial white matter. We performed the following paraclinical evaluation: Neuropsychological evaluation: MMSE "Mini Mental State Examination", FAB "frontal Assessment Battery", ISAACS Set Test, Reflexive praxis, Dubois 5-Word Test, Digit span task, Clock Test, Hachinski Score and Instrumental Activities of Daily Living. Etiological assessment of stroke: Cardio vascular assessment, lumbar puncture, HLA B51 typing, Retinal angiography, Biopsy of the salivary glands, Autoimmune check-up, Inflammatory check-up, Standard biological check-up, Thyroid check-up and serologies (HIV, TPHA, VDRL, HBS, HCV,..), Thrombosis workup (protein C, protein S, antithrombin III, protein C resistance), ....

Results:: Patient has vascular dementia secondary to hereditary thrombophilia due to partial protein C deficiency.

Conclusions:: Once protein C deficiency is detected, family investigation should be performed to prevent the occurrence of ischemic stroke.
RESTORATION OF COGNITIVE FUNCTION BY HUMAN NEURAL STEM CELLS AND MICROGLIAL CELLS ENCODING FUNCTIONAL GENES IN ALZHEIMER DISEASE MICE

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Background and Aims:: In Alzheimer’s disease patients, amyloid β peptide-mediated degeneration of cholinergic system utilizing acetylcholine for memory acquisition is observed. Since AD therapy using acetylcholinesterase inhibitors are only palliative for memory deficits without reversing disease progress, there is a need for effective therapies, and cell-based therapeutic approaches should fulfill this requirement.

Methods:: We established F3.ChAT human neural stem cells encoding choline acetyltransferase gene, an ACh-synthesizing enzyme, HMO6.NEP human microglial cells encoding neprilysin gene, an Aβ-degrading enzyme, and HMO6.SRA cells encoding scavenger receptor gene, an Aβ-uptaking enzyme. As an AD model, AF64A was selected to induce ACh depletion and cognitive dysfunction. The established NSCs and microglial cells alone or in combination were transplanted to the AD mice, and analyzed for biochemical, immunohistochemical, and neurobehavioral parameters.

Results:: Intracerebroventricular injection of AF64A induced Aβ accumulation, ACh depletion, and cognitive dysfunction of mice. ICV transplantation of NSCs and microglial cells were found to survive up to 4 weeks in the mouse brain and expressed their functional genes. Treatment with the NSCs and microglial cells encoding each functional gene restored the learning and memory function of AF64A-challenged mice by eliminating Aβ deposits and recovering ACh level. The cells also attenuated inflammatory astrocytic response by reducing Aβ accumulation. Furthermore, higher efficacies were obtained by combinational treatments of F3.ChAT and HMO6.NEP or HMO6.SRA cells.

Conclusions:: Taken together, it is expected that NSCs and microglial cells over-expressing ChAT, NEP or SRA genes could be candidates for replacement cell therapy of AD, and that their combinational treatments should be a good strategy for an enhanced effectiveness.
VISUAL RATING SCALE FOR ASSESSMENT OF THE CINGULATE ISLAND SIGN IN THE DIFFERENTIAL DIAGNOSIS OF DEMENTIA WITH LEWY BODIES AND ALZHEIMER DISEASE

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Background and Aims:: Typical brain 18-FDG PET findings in DLB consist on reduced occipital metabolism and the presence of cingulate island sign (CIS), defined by a relative preservation of the metabolism in the posterior cingulate cortex (PCC) compared with the precuneus and cuneus. We aimed to assess the utility of a semiquantitative CIS score on the differential diagnosis between DLB and AD.

Methods:: A neurologist blinded to the clinical diagnosis assessed the presence of hypometabolism in PCC, precuneus, and cuneus and thus the presence of CIS was rated as: 0 = absent; 1 = intermediate; 2 = present. The ratings from each hemisphere were summed to a visual CIS score (0-4).

Results:: 30 patients with AD (19 typical and 11 atypical, including 6 visuo-spatial variant), and 39 patients with DLB were analyzed. The mean CIS score was 0.4±0.8 for AD and 1.46±1.59 for DLB (p=0.002). CIS score 3 and 4 were found in 12 DLB and 1 AD (visuospatial variant). CIS score 0 was found in 17 DLB and 23 AD. With a defined cut-off CIS score >=2, sensitivity and specificity were 0.56 and 0.77, respectively. 6/17 of DLB with CIS 0 were in the very early stage of the disease, and 4 have concomitant posterior cingulate and precuneus hypometabolism.

Conclusions:: Visual rating of PET-CIS could differentiate DLB from AD at the higher values of the scale (CIS 3-4). Low sensitivity is expected in the early stage of the disease and in the comorbid DLB/AD cases. Atypical posterior variant of AD may have intermediate/high CIS scores.
FRONTOTEMPORAL RIGHT PREDOMINANT HYPOMETABOLISM IN BVFTD IS NOT FREQUENT AND ASSOCIATED WITH MORE SEVERE TEMPORAL ATROPHY

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Background and Aims:: Prosopagnosia, memory deficits and behavioural changes has recently proposed as the core symptoms of a further variant of frontotemporal dementia, associated with right temporal atrophy or hypometabolism and named right temporal variant (rtvFTD). Aim of the study was to evaluate frequency and clinical characteristics of patients with prevalent fronto and/or temporal right atrophy/hypometabolism.

Methods:: We revised clinical charts and neuroimaging of 52 bvFTD patients. Inclusion criteria were a diagnosis of probable bvFTD according to established criteria, presence of brain MRI and FDG-PET, full clinical history and cognitive assessment. All patients underwent neuropsychological evaluations, Neuropsychiatric Inventor (NPI) and Stereotypes rating inventory (SRI) questionnaires. Genetic analysis was assessed for all patients. Atrophy and vascular load were assessed using dedicated scales and brain hypometabolism was qualitatively evaluated on a scale from 0 to 3. Asymmetry was assigned for each lobe considering the highest values at the PET scan.

Results:: No-one patient had isolated right temporal atrophy/hypometabolism. 5 patients showed prevalent right temporal and frontal changes, 5 only frontal hypometabolism, versus 23 patients with prevalent left frontotemporal involvement. Cognitive and behavioural variables were similar between right, left or symmetric frontotemporal involvement a part from a worse memory for the left-side group. Onset with language disturbances was more frequent in left side patients. History of psychiatric disturbances was more frequent in symmetrically distributed neuroimaging abnormalities. Patients with right variant had the highest level of right and left medial temporal lobe atrophy at MRI.

Conclusions:: Prevalent right asymmetric brain dysfunction among bvFTD patients did not characterized specific phenotypes.
THE THERAPEUTIC EFFECTS OF EXERCISE ON THE COGNITIVE AND PHYSICAL FUNCTION OF PATIENTS WITH DEMENTIA

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Background and Aims:: Background and aims: Dementia is characterized by a decrease in cognitive and physical functions. Unlike in previous years, there is more interest in the role of exercise as a treatment strategy for people with dementia. The aim of this study is to investigate the effect of different types of exercise and its parameters on cognitive and physical function in patients with dementia.

Methods:: This is a study (hybrid narrative review), which includes almost all the steps of a systematic research but it is not included meta-analysis. The articles were selected through various sources such as PubMed / Medline, Scopus and Google scholar and according to additional criteria.

Results:: Were included fourteen studies with two (2) types of exercise. Aerobic exercise and mixed interventions have been studied more, while resistance interventions have been less studied. Both of the types of exercises have shown positive effects. Patients with dementia participating in aerobic exercise improved their aerobic ability and it seems to be related to changes in cognitive, neuropsychiatric symptoms and instrumental activities of daily life. Mixed exercise improved cognitive and physical function more effective than aerobic exercise alone.

Conclusions:: Conclusions: Exercise may help maintain or improve cognitive and physical function in patients with dementia but additional study is needed to clarify optimal intervention and established guidelines.
AMELIORATION OF COGNITIVE IMPAIRMENT AND NEURODEGENERATION BY NEW GENERATION PDE5 INHIBITOR IN STREPTOZOTOCIN-INDUCED EXPERIMENTAL DEMENTIA IN RATS

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Background and Aims: Background and Aim: Alzheimer’s disease is a neurodegenerative disorder that primarily depletes memory and other important mental functions. Studies reveal that PDE5 inhibitors (PDE5I) are capable of crossing Blood Brain Barrier and causes no disruption or damage. Recent studies indicates that PDE5 inhibitors can restore memory function in AD as well as non-AD models. The present study was designed to evaluate the neuropharmacological effects and mechanism of action of PDE5 inhibitor against Streptozotocin induced cognitive deficit in
Methods: Rats were pre-treated with different doses of PDE5I orally once daily for 21 days and then Alzheimer's disease was induced in the rats by bilateral ICV intracerebroventricular (ICV) administration of streptozotocin (STZ) (3mg/kg body weight) into the hippocampal region of the brain. Neurobehavioral parameters like Morris water maze test, Conditioned avoidance, Novel object recognition, Modified Y-maze, Fear conditioning, Resident-intruder aggression were assessed in the starting, at the mid and at the end of treatment. AchE activity, APP gene expression and antioxidant
parameters were studied. Histological examination of brain tissue was performed to detect presence of amyloid-beta plaques or tau protein.

**Results:** PDE5 inhibitor successfully attenuated the oxidative stress and averted the memory loss. AchE expression was decreased in ICV-STZ group and PDE5I pre-treatment improved the expression of AchE. Besides, inflammatory markers like Interleukin-6 and TNF-alpha levels were significantly reduced by PDE5I pre-treatment.

**Conclusions:** Conclusion: Our data is suggestive of promising role of PDE5I in preventing memory loss, ameliorating the oxidative stress and might be beneficial for the treatment of Alzheimer's disease.
MILD COGNITIVE IMPAIRMENT (MCI): EVOLUTIONARY DIVERSITIES IN 40 PATIENTS. AN ALGERIAN STUDY.

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Background and Aims:: Patients with MCI have a memory complaint with preserved autonomy. Nevertheless, this memory impairment remains inferior in comparison with the memory of a healthy subject of the same age. Several evolutionary nosological frameworks are possible: from normal cognitive ageing, through the so-called stable MCI, to dementia (in unstable MCI). The aim is to give the clinical and evolutionary characteristics of a sample of an Algerian population of 40 patients with an MCI phenotype and followed for a minimum of 5 years.

Methods:: Retrospective study with analysis of demographic data, measurement of cognitive functions at the time of diagnosis and on several occasions during the evolutionary follow-up. A detailed neurological examination as well as an exhaustive paraclinical assessment (biological and radiological) were also performed. 6 patients underwent a lumbar puncture with study of the biomarkers of Alzheimer’s disease.

Results:: Among the 40 patients studied, 11 (27.5%) had a stable, non-progressive MCI. 13 patients (32.5%) had an unstable form that evolved into dementia. In addition, 8 patients (20%) had normal cognitive ageing, 3 ones (7.5%) developed a depressive syndrome and 3 (7.5%) had a vascular form. 1 patient (2.5%) had a vitamin B12 deficiency and 1 patient (2.5%) a probable para-neoplastic form associated with Hashimoto's autoimmune thyroiditis.

Conclusions:: The results of this Algerian series demonstrate the heterogeneity of the evolution of MCI patients, and raise the interest of early diagnosis of possible other clinical signs (other cognitive domains) and/or biological signs (positive biomarkers) that may be precursors of dementia and already present at the MCI stage.
Background and Aims:: Background: Epilepsy is a well-known neurological disorder. Seizure severity emerges as an important aspect of epilepsy. The severity of seizures depends on many factors which can affect the patient's disease control and management. Aims: To assess seizure severity among patients with epilepsy attending Daoud charity clinic.

Methods:: A descriptive clinic based cross sectional study was performed using seizure severity assessment scale. 99 patients with epilepsy who attend Daoud charity clinic were included in the study between the period of 2019 to 2020.

Results:: Out of 99 patients, 66 (66.7%) were females and 33 (33.3%) were male. The most common age of the patients ranges from 15 to 31 years (67.7%). Almost 75 of the participants have generalize epilepsy (generalized tonic colonic (69.7%), myoclonus (3%), absence (3%)). 24 had focal epilepsy (21(21.1%) focal with impairment and 3(3%) focal without impairment). The patients who participated in the study had the following seizures severity assessment, very mild seizures (7.7%), moderate mild seizures (3%), mild seizures (11.1%), moderate seizures (6.1%), moderate severe seizures (19.2%), severe seizures (14.1%) and very severe seizures (18.2%).

Conclusions:: The study showed that epileptic seizures have different degrees of severity, and can be classified according to their severity. This type of classification can help a lot in the process of treatment, and taking into consideration different psychological issues in corresponding with the severity of seizures.
ANTIEPILEPTICS' DRUG RESPONSE AND SCN2A MUTATIONS IN SUDANESE PATIENTS WITH IDIOPATHIC EPILEPSY.

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Background and Aims:: Sodium channel blockers are widely used for epilepsy in Sudan however some patients don’t respond to them. Since SCN2A mutations have a role in idiopathic epilepsy why does resistance develop? Aim: To detect SCN2A mutations and study their relation to Antiepileptic drug response.

Methods:: 28 patients from the National Center for Neurological Science (NCNS) and 71 from prof Doud clinic were selected during the period between September /2016 and February /2019. Their genetic profiles were investigated by ABGI sequencing and different bioinformatics soft-wares (blast NCBI, Bioedit software, mutation taster, and chimera software version 1.14.

Results:: These frameshift mutations at exon 2 near to the N –terminal mutations were detected: I25Ifs*68, E26nfs*67, and A23Ifs*70. They lead to change in the protein structure, and affect the drug-receptor binding. The last one was unique because it was detected in poor drug response patient and was not found even in his brother genetic profile (who have the same class of seizure but respond well to treatment) it may be behind the reduction in drug response, the mutation modifies the non-reactive Alanine to Leucine. It is a truncated protein mutation that will reduce the number of Na channels affecting drug-receptor binding.

Conclusions:: Since sodium channel blockers are the commonly used antiepileptic's in Sudan, there is a strong need to identify patients with SCN2A defect to modify their modality of treatments.
CLINICAL PREDICTORS FOR ANTIEPILEPTIC’S DRUG RESPONSE AMONG IDIOPATHIC EPILEPSY PATIENTS IN SUDAN

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Background and Aims:: Epilepsy was documented firstly by prof Daoud Mustafa (peace upon him) and prof Basheer Arbab in 1961 as a case report. This was followed by studing its clinical presentation, its pattern, treatment safty and efficacy ended with working through refractory epilepsy in tertiary center. AIM : To identify the clinical prognostic factors of idiopathic epilepsy among Sudanese patients.

Methods:: there were 71 patients with idiopathic epilepsy recruited from Prof Daud clinic , Osman Saleh Center, Omdurman, Khartoum state, Sudan; and 28 patients from NCNC ,Ibrahim Malik hospital, Khartoum between August 2016 and February 2019. Their demographic data, seizure characteristics, drugs, and concomitant conditions were recorded in dc-hoc forms. The data was analysed using excel and SPSS program .

Results:: over all response to treatment was good in 89%. This response was associated insignificantly with age group above 65 years, focal seizure, duration less than 5 years, or mono-therapy while frequency of seizure pretreatment and good response to first regiment has significant statistical response.

Conclusions:: There was good response to treatment especially if there was low seizure frequency before the intiation of treatment, and the patient respond well to the first treatment regimen.
Background and Aims:: Acute symptomatic seizures (ASS) are defined as clinical seizures that occur in an acute temporal relationship with the central nervous system (CNS). It is possibly due to several acute conditions. This study aims to describe profile of patients with acute symptomatic seizures.

Methods:: This is a descriptive cross sectional study of ASS patients in neurology ward of Moehammad Hoesin Hospital, 1 April-31 June 2019. A sample was patients >= 18 years old, experienced seizures that was provoked by acute conditions and EEG was performed before 7 days after seizure.

Results:: There were 62 samples. Most were women (56.45%). The highest age range is 40-69 years (64.52%). It is because the incidence of ASS increases progressively after 35 years old and for ASS with stroke especially increases in the 50-69 year age group. The most common type of seizure was general tonic clonic (37.10%). Most etiology was vascular (41.93%) then malignancy and other causes. Most of the EEG result were slowing (26%). Normal EEG were 30.64%, but not all of them had good clinical outcomes or no sequelae. Only 2 people who died with the etiology of stroke and sepsis. Both EEG are slowing with epileptiform discharge.

Conclusions:: The incidence of ASS increases in older age group as the incidence of acute underlying disease increases. The clinical outcome is determined by the severity of acute condition present. It may be because increased glutamate and aspartate during a brain injury trigger a seizure.
EEG RESTING-STATE NETWORK AND FUNCTIONAL CONNECTIVITY ANALYSIS IN SUBJECTS WITH PSYCHOGENIC NON-EPILEPTIC SEIZURES

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Background and Aims:: Psychogenic non-epileptic seizures (PNES) are hypothesized to be related to functional brain network abnormalities.

Methods:: To test this hypothesis, we used an approach based on power spectral density (PSD) and graph theory to study whole-head surface connectivity by resting-state electroencephalography (EEG) of 20 participants with PNES and 19 unaffected controls. We also investigated synchronism between pairs of EEG electrodes and between inter-hemispheric brain areas using the phase lag index to develop readable synchronization bi-dimensional maps for an objective overview of changes in functional connectivity associated with scattered cortical abnormalities.

Results:: Compared with controls, participants with PNES showed some changes in the power spectral distribution, with notable alteration in the frontal lobe, a lateromedial trend in the delta and theta bands (p=0.002), and significant changes in the right central/left parietal regions in the alpha and beta (p=0.002) ranges. Participants with PNES also showed widespread changes in network metrics compared with controls, including decreased global efficiency, increased cluster coefficients, and shorter path lengths compared to controls.

Conclusions:: Our results suggest that PNES is associated with decreased prefrontal and parietal synchronization, possibly reflecting dysfunction of networks within these regions.
Background and Aims:: Epilepsy therapy is always chronic and often uses more than one drug. Almost 80% of patients experience adverse effects. It is a major cause of failure of treatment. This study aims to describe the adverse effects of antiepileptic drugs (AED) at neurology clinic, Muhammad Hoesin Hospital.

Methods:: This is a descriptive analytic study between 1 October to 31 December 2020. Inclusion criterias were epilepsy patients aged ≥ 18 years who have taken certain AED and same dose in the last 1 month. Data collected using the Liverpool adverse effect profile and the Naranjo questionnaire.

Results:: Of the 41 subjects, 30 patients (73.2%) experienced AED adverse effects. Most of patients had no more seizures (70.7%) and had consumed AED for ≥12 months (56.1%). Subjects with monotherapy were 48.8% and the most using phenytoin. The most polytherapy combinations were phenytoin and valproic acid. Subjects who used polytherapy experienced adverse effects were 85.7% and had a 1.43 times greater risk of adverse effects than monotherapy. The number of AED has a significant effect on side effects occurrence, both in bivariate (p 0.031) and multivariate analysis (p 0.038 OR 4.90 CI 95%). Common adverse effects include memory problems, drowsiness, difficulty concentrating, fatigue, and irritability. This is related to the most widely used AED, namely phenytoin, valproic acid, levetiracetam, and carbamazepine.

Conclusions:: Patients who used polytherapy experienced adverse effects had 1.43 times greater risk than monotherapy. Common adverse effect was memory problems.
COMPARING EPILEPSY TO PSYCHOGENIC NON-EPILEPTIC SEIZURES, IDENTIFICATION OF RISK FACTORS: A RETROSPECTIVE CASE-CONTROL STUDY

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Background and Aims:: Psychogenic Non-epileptic seizures (PNES) are commonly misdiagnosed as epilepsy. Approximately 20% of patients sent to epilepsy centers for intractable seizures were later confirmed with PNES, resulting in incorrect treatment and medical cost. The objective of this case-controlled study is to identify factors associated with the development of PNES.

Methods:: A retrospective case-control study was conducted at a Hawaii epilepsy center from 2014-2020. 101 patients with PNES were identified. Patients' socioeconomic and biopsychosocial co-morbidities were recorded. Four epilepsy patients were randomly selected per each PNES patient comparison. Statistical analysis was performed using univariant nonparametric tests, and multivariable logistic regression.

Results:: Odds of PNES in females was 2.34 (p=0.00046). Median age in PNES was 43 (30, 54) and 51 (33, 66) in epilepsy, p=0.00037. Medium household income in PNES was 77188 (59284, 100311), and 82742 (70110, 100311) in epilepsy, p=0.024. Statistically significant psychiatric variables: illicit drug use (p=0.00017), anxiety (p=9.39*10^-14), depression (p=7.76*10^-7), PTSD (p=5.44*10^-7), ADHD (p=0.030), and bipolar disorder (p=0.0089). Statically significant biological factors: median BMI (p=0.051), history of stroke (p=0.028), history of TBI (p=0.030), asthma (p=3.29*10^-5), migraines (p=7.18*10^-7), and chronic pain (p=0.013). Multivariable logistic regression identified the strongest predictors of PNES: females (p=0.026), drug use (p=0.014), anxiety (p=2.93*10^-5), PTSD (p=0.024), BMI (p=0.020), and traumatic brain injury (p=0.052).

Conclusions:: PNES patients are predominantly female, eight years younger, and have lower income. They have higher odds of psychiatric factors: illicit drug use, anxiety, depression, PTSD, ADHD, and bipolar disorder; and higher BMI and odds of certain biological factors: stroke, traumatic brain injury, asthma, migraines, and chronic pain.
AN ALGORITHM FOR CALCULATING KETOGENIC DIET PARENTERAL NUTRITION IN REFRACTORY EPILEPSY

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Background and Aims:: Refractory epilepsy is the most prevalent neurologic condition with significant morbidity and economic burden. Ketogenic diet parenteral nutrition (KD-PN) was a considerable choice for them when enteral feeding is limited temporarily. Objective was to create a computer based algorithm for accurate component calculating, with the aim to help doctors to tailor the dietary prescription

Methods:: The computer-based algorithm based on ESPGHAN/ESPEN/ASPEN guidelines and optimal clinical management of KD/KD-PN mainly. Summarize the formulas of energy, fluid, protein, lipid, carbohydrates, electrolytes, vitamins, and trace elements. relevant parameters include height, weight, age, gender, and VCO2 (if mechanically ventilated), etc. Conclude the specification, concentration, calorie, osmolar of each parenteral nutrition (PN) by instructions, parameter is volume. Edit formulas and parameters into Excel

Results:: The computer-based algorithm of energy (kcal/d) was calculated by formula 8.19×VCO2 (ml/min) or weight-based formula 20–65×weight(kg). The amino acids intake of 0.6–2.0 g/kg/d was considered for most patients, it was mainly affected by different phases of disease and age. Fat-intake not exceeding 4 g/kg/d. Reduced supply of carbohydrate is limited by the quantity of protein and lipids. the intake of electrolytes, vitamins and trace elements mainly affected by age and weight. The detailed dates of each PN, diet ratio, osmolar, etc were determined by the datas above.

Conclusions:: we provides a new computer based algorithm for accurate component calculating, with the aim to help doctors to tailor the dietary prescription of KD-PN according to individual PN needs.
LATE ONSET EPILEPSY IN CEREBRAL AMYLOID ANGIOPATHY PATIENTS: A CASE CONTROL STUDY

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Background and Aims:: Sporadic cerebral amyloid angiopathy (CAA) is characterized by amyloid deposition in the walls of leptomeningeal and cortical arteries, arterioles of the central nervous system. To date, epileptic seizures at CAA onset have rarely been reported and its prevalence is unknown. In reason of the high frequency of CAA in the elderly population and of the expected epileptogenic role of cortical hemorrhagic lesions, it may be hypothesized that CAA can explain a proportion of late-onset epilepsies with unknown etiology. This study aims to assess the possible correlation between CAA and late onset (>55 years) epilepsy.

Methods:: We have consecutively included patients with late-onset epilepsy (defined as seizure onset after 55 years) and age-matched controls who underwent brain MRI for reasons different from epileptic seizures. All subjects underwent 1.5 Tesla MRI including: axial T1-weighted, T2-weighted, 3D fluid-attenuated inversion recovery (FLAIR), DWI images, Gradient-echo and/or SWI images. In patients with epilepsy, MRI has to be performed within 30 days from epilepsy onset. In order to evaluate differences between groups, Chi-squared test is performed.

Results:: To date, we have included 20 patients with late onset epilepsy (15 males, mean age 73 ± 8 years) and 44 age-matched controls (15 males, mean age 69 ± 8 years). CAA is significantly more frequent (p=0.01) in patients with late onset epilepsy (4/20) than in controls (1/44).

Conclusions:: These preliminary data demonstrate that CAA is more frequent in patients with late onset epilepsy than in age-matched controls.
ENHANCING MEMORY AND QUALITY OF LIFE THROUGH NOVEL HOME-BASED NEUROPSYCHOLOGICAL REHABILITATION FOR EPILEPSY: A RANDOMIZED CONTROLLED TRIAL

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Background and Aims:: Memory impairment in epilepsy is a critical determinant of Quality of Life (QoL). Subjective complaints may reflect depression. 6-week home based Neuropsychological Rehabilitation (NR) program was developed for patients with Drug Refractory Epilepsy (DRE) [Post-Operative (PO) & Not Cleared for Surgery (NCS)]. This includes psychoeducation, compensatory training and cognitive retraining aimed at improving memory. Neuropsychological outcomes were studied.

Methods:: 27 adults with DRE were recruited in a single blind RCT (CTRI/2019/10/021777) with 14 patients in the Intervention (IG) (PO=13, NCS=1), and 13 in the Treatment As Usual (TAU) (PO=11, NCS=2) groups. They were aged 18-45 years with minimum primary level of education, IQ > 80 and available primary caregiver. Pre-post neuropsychological assessment included Auditory Verbal Learning Test, Everyday Memory Questionnaire (EMQ), Hamilton Depression Inventory and Quality of Life in Epilepsy-31. Due to COVID-19, a booster session (focused on internal & external aids) was given at 3 months and all follow-ups were done through tele-assessment at 6 months.

Results:: At baseline, there was no significant difference between the groups on objective and subjective measures. Linear regression analysis post adjustment for depression at follow-up revealed a significant difference between the groups on objective cognitive measures of learning (p=0.019), delayed recall (p=0.003), retention (p=0.045) with IG showing higher performance. Similar results were noted for subjective measures of EMQ (p=0.001) and cognitive (p=0.001), seizure freedom (p=0.030), overall QoL (p=0.046) subdomains of QoL with its total score (p<0.001).

Conclusions:: Despite depression, IG reported higher performance on objective tests, lower subjective complaints and better QoL at long term follow-up.
THE STUDY PSYCHOLOGICAL STATUS IN EPILEPTIC PATIENTS WITH DIFFERENT EEG LOCALIZATION OF PAROXYSMAL ACTIVITY

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Background and Aims:: The study of the cognitive, emotional-behavioral characteristics in adults patients with epilepsy (PE) with different lateralization of EEG paroxysmal activity (PA).

Methods:: 79 PE were examined, all underwent of EEG. Groups were distinguished: 1st - PA in the right hemisphere (38 PE), 2nd - PA in the left hemisphere (41 PE). Cognitive, emotional-behavioral spheres are studied using the battery of psychological techniques.

Results:: Cognitive-sphere: 1st group - instability of attention, errors in the digital proofreading sample-26.6, reduced scale assessment “Encryption” of the Wexler-7.7, 2nd group - 22.5 and 9.0, respectively (p<0.5). Emotional-behavioral: 2nd group are prone to polar emotional response, the “Activity” factor of the “SDF” - 3.3, the impulsivity scale of the MMPI-method - 65.6, in 1st group 1.5 and 70.2, respectively. In the 1st group, there is a reliable correlation between the indicators of the impulsivity and anxiety scale of the MMPI (r = 0.46, p≤0.05). The 2nd group choose non-adaptive emotional-behavioral strategies according of E. Khaimah - 32.1% and 28.6%, in 1st group - 17.9%; 14.3%, respectively.

Conclusions:: The attrition of the dependence of psychological parameters in epilepsy on PA is due to the prevailing of neuronal activity disorders determined in the structure of both single-focal and multifocal epileptic discharges. The level of involvement of hemispheric regions in the epileptic process masks the connection of psychological indicators with PA.
DIFFERENTIATION OF OCCIPITAL EPILEPSY FROM MIGRAINE HEADACHE WITH AURA: A COMPARATIVE ANALYSIS OF THE PATIENTS PRESENTED IN A TERTIARY CARE CENTER OF BANGLADESH

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Background and Aims:: Occipital epilepsy is relatively uncommon and probably underdiagnosed, often misdiagnosed as migraine with aura. Early diagnosis requires clinical suspicion which leads the neurologist to advice electroencephalogram (EEG) and brain imaging, which are unnecessary in case of migraine with aura.

Methods:: We documented the patients presented in the department of Neurology, Dhaka Medical College from June, 2019 to January, 2020 with confirmed occipital epilepsy, presented with visual semiology, EEG changes and or structural abnormality in the occipital region. We compared the ictal visual hallucination with the aura of 18 confirmed patients with migraine.

Results:: We found 10 confirmed patients with occipital epilepsy with median (IQR) age was 22 (15-47) years, mostly female [8(80%)]. The etiology seems to be idiopathic in 3 patients. Among the symptomatic patients pathologic abnormality found in the occipital regions included, space occupying lesion, post hypoxic damage, post stroke encephalomalacia, gyral calcification due Sturge weber syndrome and Wilson's disease. EEG findings included focal or generalized epileptiform discharges and occipital rhythmic intermittent delta activity (ORIDA). The visual hallucinations included transient [median (IQR), 35(3-375) seconds] flushing of the light, formed visual hallucination and bright dots of colored lights. Where as in aura of the migraine colorless bright dots, scintillating scotoma and transient visual blurring were dominant. The ictal visual hallucination was associated with compressive headache [9(90%)], tinnitus [5(50%)], ictal vomiting, photophobia and phonophobia. In 6 (60%) instances there were associated convulsions.

Conclusions:: Patients presented with very transient, distinct elementary visual hallucination and associated convulsion warrant evaluation for occipital epilepsy.
A CASE OF EPILEPTIC “BELLY DANCING”

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Background and Aims:: The “belly dancing” phenomenon is featured by undulating movements of the abdominal wall. Although several aetiologies have been reported, the epileptic origin is the most commonly described. Previously reported patients were known to have epilepsy, were already receiving antiepileptic drugs, presented with focal status epilepticus, and/or their seizure motor phenomenology also included the eyes, face, limbs, and even loss of awareness. Isolated epileptic “belly dancing” has been very rarely described so far.

Methods:: A 60-years-old man, with one-year history of lung adenocarcinoma (ACL-T1cN2M0, stage IIIa, TTF1+, p40-), presented with a cluster of self-limited, short-lasting (~one minute), involuntary, clonic-like contractions (1-2Hz) involving abdominal muscles on the right side, occurring at interval of 40-60 minutes. There was no loss of awareness.

Results:: Neurological examination was normal. Inflammatory and autoimmune work-up was unremarkable. Prolonged video-EEG/EMG polygraphy monitoring demonstrated interictal epileptiform EEG activity and documented a focal seizure of left centroparietal origin accompanied by surface EMG bursts activity recorded from right rectus abdominis muscle (Figure 1). Brain MRI revealed left parietal metastatic brain tumor at the gray–white junction with surrounding vasogenic edema (Figure 2). After intravenous administration of levetiracetam (500 mg bid), no further seizures were observed.
Conclusions: In most previous reports as in our case, the “belly dancing” epileptogenic zone correspond to the mesial frontal and/or parietal areas around the central sulcus, in agreement with the trunk somatotopic representation. The limited representation of abdomen and the overlapping representations of body parts over the sensory/motor homunculus, may account for the rarity of isolated epileptic “belly dancing” phenomenon.
IRF2BPL NONSENSE MUTATION ASSOCIATED WITH ADULT ONSET MYOCLONIC EPILEPSY AND CEREBELLAR ATAXIA: A CASE REPORT.

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Background and Aims:: The Interferon Regulatory Factor 2 Binding Protein-Like (IRF2BPL) is a recently discovered gene, whose mutations are associated with heterogeneous neurological phenotypes, in most cases developmental and epileptic encephalopathies. We present the case of an IRF2BPL mutation associated with adult-onset myoclonic epilepsy and cerebellar ataxia.

Methods:: A 22 years-old female patient with mild learning disabilities developed a progressive decline in cognitive and motor functions, manifesting mental slowness, forgetfulness, unsteady gait with frequent falls, mild speech ataxia, action tremor, myoclonic jerks, and a single generalized tonic-clonic seizure. Family-history was negative, and brain imaging together with laboratory tests were normal. Prolonged EEG showed diffuse epileptiform abnormalities, frequent multifocal myoclonus, and a photo-paroxysmal response. The myoclonic jerks improved with Levetiracetam and Clonazepam, while cognitive and motor impairment persisted.

Results:: Whole-exome-genome sequencing showed a never-before-described heterozygous nonsense mutation (c.364C>T, p.Gln122Ter) in the IRF2BPL gene. Leading to the insertion of a premature STOP codon, this mutation is considered potentially pathogenic according to updated recommendations.

Conclusions:: IRF2BPL mutations are mostly associated with severe neurological regression. Our patient showed a different phenotype, resembling the clinical features of Progressive Myoclonic Epilepsy (PME): myoclonic jerks, seizures and progressive neurologic impairment. Although the most common PME phenotypes are attributed to specific genetic defects, almost 30% of PMEs are of undetermined cause and this is the first report of an IRF2BPL mutation. Our report needs confirmation by further studies; however, it contributes to the knowledge of the heterogeneity of the IRF2BPL-mutations phenotype and suggests that it should be considered in patients with PME.
ROLE OF INTENSITY OF ELECTRICAL STIMULATION (ES) IN THE CEREBELLAR ANTIEPILEPTIC EFFECTIVENESS UNDER CONDITIONS OF DIAZEPAM ADMINISTRATION

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Background and Aims:: Background. ES of brain structures combined with antiepileptic drugs is a promising approach for better pharmacological control of resistant seizures. Aims. To investigate the dynamic of penicillin-induced foci in cats’ brain cortex under conditions of paleocerebellar electrical stimulation (ES) delivered at different intensities and diazepam administration.

Methods:: Methods. Via penicillin solution (20.000 IU/ml) application upon posterior sigmoid gyrus epileptic foci have been created in anesthetized, myorelaxed, and artificially ventilated cats. ES of paleocerebellum (100 Hz, 1 ms, duration of trial 1 s) have been delivered to VI lobula of paleocerebellum with two bandwidths of intensities: 80-150 mcA (lower) and 200-500 mcA (higher) ones. Diazepam was administered in dose 2.0 mg/kg, i.v.. The monopolar EEG was registered, and i.v. saline administration to animals was used as control.

Results:: Results. The frequency of epileptic discharge generation at the maximal level of epileptic activity was 25-40 discharges per min. During ES delivered at a lower intensity, the decrease of discharges frequency by two-three times was observed. Higher frequency of ES induced activation of spikes generation up to 50-75 per min. In 30.0 min from the diazepam administration and 20 min from the moment of restoration of focal activity via additional penicillin application, lower intensity ES did not modulate spikes generation, while higher intensity caused up to twice reduction of spikes frequency or complete suppression of focal activity.

Conclusions:: Conclusions. Modulative effects of paleocerebellar ES on cortical penicillin foci depend on its intensity. Diazepam in high dose abolished effects of low-intensity ES while higher intensity induced suppression of epileptic activity.
THE EFFECTS OF ANTI-EPILEPTIC DRUGS ON HIGH-FREQUENCY OSCILLATIONS IN SOMATOSENSORY EVOKED POTENTIALS

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Background and Aims:: High frequency oscillations (HFOs) of Somatosensory evoked potentials (SEPs) reflect the activity of thalamo-cortical and cortical neurons from the sensory pathway. Antiepileptic-drugs (AEDs) reduce seizures acting on the balance between excitation and inhibition. We aimed to study the effect of AED mono and polytherapy on SEP-HFO's components

Methods:: Twenty-five patients with focal epilepsy were enrolled for the purpose of this study. Patients were divided in 3 groups according to the number of AEDs (1, 2 or 3 AEDs). Patients in group 1 underwent SEP-HFOs recording in drug naïve condition and at 1 month after AED titration. HFOs were compared in duration, amplitude and latency among the three groups.

Results:: The amplitude and duration of late HFOs of the affected hemisphere (AH) are different between groups and inversely correlated with the number of AEDs. In naïve patients mono therapy reverts the asymmetry in totHFOs (total HFOs) duration.

Conclusions:: Our results demonstrate that SEP-HFOs are sensitive to the action of AEDs on cortical excitability. This effect seems to affect mainly the cortical component of HFOs in the AH and it is related to the number of AEDs taken. Significance: SEP-HFOs might be a viable tool to probe cortical excitability changes induced by AEDs. © 2020 International Federation of Clinical Neurophysiology
THE USE OF OPTICALLY PUMPED MAGNETOENCEPHALOGRAPHY (OP-MEG) IN EPILEPSY

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Background and Aims:: Magnetoencephalography (MEG) has been used in specific cases of refractory epilepsy due to its inherent properties of excellent spatial resolution and relative immunity to muscle artefact. However current MEG systems are high maintenance and restrictive for the patient, meaning that recording sessions are usually brief (1-2 hours), thereby limiting its availability in the clinical setting. Our aim was to demonstrate the first use of Optically Pumped Magnetoencephalography (OP-MEG) in two epilepsy patients with unrestricted head movement. Unlike conventional MEG that uses a superconducting SQUID system, here we use a different type of sensor (OPM), which operates at room temperature and crucially can be placed directly on the patient's scalp, permitting free head movement.

Methods:: We performed three OP-MEG recording sessions in two patients with refractory focal epilepsy (right posterior temporal focus in patient 1 and left frontal focus in patient 2), who were able to perform natural movements within their environment. We then compared these recordings with clinical scalp EEG performed earlier. In the second patient we also incorporated motion capture in order to regress out head movement from the MEG signal.

Results:: OP-MEG was able to identify analogous interictal activity to scalp EEG including spikes, polyspikes, sharp waves and spike and wave activity. We were able to source localise this activity using both linearly constrained minimum variance (LCMV) beamformer and equivalent current dipole (ECV) methods to an appropriate brain region.

Conclusions:: This is the first application worldwide of OP-MEG in human epilepsy. Future directions include simultaneous EEG/OP-MEG recording and prolonged OP-MEG telemetry.
Background and Aims: Background. The suppression of epileptic activity follows TDCS. It was shown that blocking peroxisomal proliferator-activated γ-receptors (PPARγ) with BADGE, (100 mg/kg, i.p.) prevented antiseizure effects caused with cerebellar TDCS (Godlevsky L.S., Pervak M.P., 2019). Aim. To investigate effects of cerebellar TDCS under conditions of treatment with the agonist of PPARγ pioglitazone upon pentylenetetrazol (PTZ) - kindled seizures.

Methods: Methods. In rats the kindling was induced via PTZ (35.0 mg/kg, i.p.) for three weeks. TDCS was performed at 250 μA intensity for 10.0 min, with cathode on the skull surface oriented to the cerebellar cortex. Pioglitazone (100.0 mg/kg) was administered i.p. in 30 min before TDCS.

Results: Results. TDCS caused the tendency to increase the latency of first seizures by 26.3% when compared with control (70.89+14.20 s) (P>0.05) and reduced the seizure severity to 3.62+0.92 from 4.22+0.67 points in control (P>0.05). Pioglitazone (100.0 mg/kg i.p.) increased the latency by 31.4% up to 103.38+17.08 s (P<0.05) and seizures were reduced to 3.5+0.76 points (P>0.05). TDCS in rats treated with pioglitazone (100.0 mg/kg, i.p.) resulted in increasing the latency by 42.2% (P<0.05) (up to 122.7+31.84 s) and reduced seizures by 31.3% (P<0.05) (up to 2.9+0.74 points). Both TDCS and pioglitazone did not affect the length of ictal potential delivered separately. The length of ictal potential was shortened by 45.0% (P<0.05) (up to 15.92+9.66 s) when TDCS was performed after pioglitazone administration.

Conclusions: Conclusions. Under conditions of treatment with pioglitazone paleocerebellar, TDCS caused pronounced antiseizure effects. That leads to the role of PPARγ in the realization of cerebellar antiseizure action.
Background and Aims:: To determine the frequency and demographics of types of epilepsy presenting to a neurology outpatients facility in a private tertiary care JCIA Accredited University hospital in Islamabad, Pakistan.

Methods:: We extracted the data from our neurology outpatient database registry from July 2014 to November 2018. This registry is approved by the Institutional Review board and Ethics committee of our hospital. A patient was diagnosed with epilepsy if there was clear evidence of recurrent epileptic seizures, with the documentation being made by a neurologist on a standard diagnostic database form.

Results:: Out of 10,047 recorded in this time period, 1,265 patients (12.6%) had epilepsy, 57.9% were male and 42.1% were female with a mean age of 25.77 ± 16.6 years. Focal epilepsy with or without secondary generalization was the most common type, seen in 49.1% of cases, with mean age of 26.35± 17.2 years with 61% males; followed by generalized epilepsy in 45.2% with almost similar age (25.85 ± 16.2 years) and gender distribution (56.3% males vs 43.7% females). Juvenile Myoclonic epilepsy constituted 3.5% cases (mean age 25± 12). Lennox –Gastaut Syndrome (LGS) was seen in 1.1%; Benign partial epilepsy with centro-temporal spikes in 0.4%; febrile seizures in 0.4%; West Syndrome in 0.1%; and epilepsy not specified in 0.2% cases.

Conclusions:: The most common epilepsy was focal epilepsy with or without secondary generalization followed by generalized epilepsy and epilepsy in general is more common in males than females.
DRUG-RESISTANT EPILEPSY SECONDARY TO PERINATAL DAMAGE: DO INTERICTAL EPILEPTIC DISCHARGES MATTER?

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Background and Aims: Perinatal damage represents a frequent cause of drug-resistant epilepsy (DRE). Abnormal EEG findings have been described as a risk factor for DRE. Our aim was to explore the relationship, if any, between interictal epileptic discharges (EDs) and drug responsiveness in epilepsy secondary to perinatal causes.

Methods: We selected patients with focal epilepsy due to perinatal events from our Adult Epilepsy Centre database. DRE was defined as proposed by the International Ligue Against The Epilepsy (ILAE). Ambulatory EEG findings for each patient were classified by the presence or absence of interictal EDs.

Results: We recruited 53 patients, 33 men and 20 women aged 42.2 (SD, 11.7) years. Twenty-four patients had DRE. Patients who responded to drug treatment and those who did not were similar for age and sex but differed for interictal EDs that were more frequent in the DRE group (15/24 vs. 10/29; Pearson Chi square, p=0.04).

Conclusions: Among patients with epilepsy secondary to perinatal damage, EDs during ambulatory EEG are more frequently encountered in drug resistant patients. In this group, ambulatory EEG may be not only a diagnostic aid but may also have prognostic value.
SKULL-BASE TEMPORAL ENCEPHALOCELE: HIDDEN CAUSE OF TEMPORAL LOBE EPILEPSY

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Background and Aims:: Among patients with Temporal lobe epilepsy (TLE), up to 30% can have normal (non-lesional) MRI scans. With increased use of high resolution MRI (3T) scans, many of the MRI-negative TLE cases turn out to be lesional TLE. Skull-base temporal encephalocele (TE), has to be suspected and specifically searched for among patients with apparent MRI negative TLE. The study aims to analyse patients with TLE for temporal lobe encephalocele.

Methods:: Patients with previously diagnosed MR negative TLE on long term video EEG monitoring were re-evaluated with 3T MRI brain over a period of 2 years (1st January 18-1st January 20) from a tertiary level comprehensive Epilepsy care centre to discover skull base temporal encephalocele.

Results:: Total 1024 VEEG were analysed. TLE was diagnosed in 104 patients based on semiology, Ictal, Interictal EEG data and brain PET studies. Out of 104 TLE patients, 99 patients had temporal lobe abnormality (78 patients had MTS, 8 patients had tumor, 3 patients had FCD, 10 patients had mixed pathology). Out of the 5 MR negative TLE patients, 2 patients were diagnosed with temporal encephalocele on subsequent high resolution 3T MR brain scans and one patient underwent EcoG guided tailored resection for complete removal of epileptogenic tissue with Engels class I seizure freedom at 1 year follow up.

Conclusions:: We propose that temporal lobe encephalocele (TE) should be searched for, as a cause
of refractory TLE, using high-resolution MRI sequences. PET positivity with an apparent negative MRI in patient presenting with TLE, should encourage one to search for TE.
CENOBAMATE AS ADJUNCTIVE THERAPY IN ADULTS WITH UNCONTROLLED FOCAL SEIZURES: TIME TO ONSET OF EFFICACY DURING TITRATION

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Background and Aims:: Cenobamate is a new antiseizure medication (ASM) approved in the US for uncontrolled focal (partial-onset) seizures in adults. Two international, double-blind, placebo-controlled trials (C013/C017) demonstrated cenobamate efficacy and safety. Here we report time to onset of efficacy during titration of cenobamate in these studies.

Methods:: Adults with uncontrolled focal seizures and taking 1-3 concomitant ASMs were enrolled in Study C013 and C017. Concomitant ASM changes were not allowed during the double-blind period. Time to onset of efficacy in patients receiving cenobamate versus placebo was evaluated during the 6 weeks of cenobamate titration (Table 1). Post-hoc analysis of efficacy examined the percent reduction in seizure frequency from baseline to each week during titration using a Wilcoxon rank-sum test (C013) or an ANCOVA model fit to the ranked values of baseline seizure rate and treatment group (C017).

Results:: Patients receiving cenobamate had significant reductions in median percent seizure frequency versus placebo starting from the first 1-2 weeks of cenobamate titration at the initial dose of 50 mg/day (C013: -26.7% cenobamate vs -15.1% placebo, P<0.05; C017: -36.4% cenobamate vs -20.0% placebo, P<0.05). Sustained significant decreases in seizure frequency versus placebo were seen throughout the 6-week titration in both studies. The median reduction in seizure frequency was progressively higher with increasing cenobamate doses of 100, 200, and 400 mg/day.

Conclusions:: Onset of cenobamate efficacy in significantly reducing seizure frequency occurs early and at lower doses than the target dose for maintenance therapy and it improves at higher doses.
A REAL-WORLD STUDY TO EVALUATE EFFICACY AND QUALITY OF LIFE OF PEOPLE WITH EPILEPSY ATTENDED OUTPATIENT DEPARTMENT OF EPILEPSY FOUNDATION

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Background and Aims:: Epilepsy can have serious physical, psychological, and social consequences, and it can have a greater impact on a person's quality of life (QOL) than chronic conditions. People with epilepsy have been shown to have lower QOL because they are more likely to have low self-esteem, anxiety, and depression. Epilepsy Foundation runs the Epilepsy clinic to provide the comprehensive care to these patient

Methods:: It is prospective, observational study to evaluate the efficacy and QoL of life of people with Epilepsy. The efficacy parameters are collected through the case record form and QoL life data is collected by 1:1 interaction with patients and later, through the periodic phone calls. The data is collected from 2018 to 2021.

Results:: Total 72 patients were enrolled in to the trial. 53% are male and 47% are female with mean age 32.23 ± 12.5. our OPD, the majority of patients are less educated, with only 18% completing high school. 8 people, 18, 26 people, and 20 people have had epilepsy for more than 30 years, 21-30 years, 10-20 years, and 10 years, respectively. In the last four years, 64% of patients have achieved seizure freedom. Because of the comprehensive management provided by the Epilepsy Foundation, the majority of patients improved in their Quality of Life.

Conclusions:: Comprehensive approach provided by Epilepsy foundation improved the Epilepsy outcomes and QoL life of People with Epilepsy. The free medication provided by Epilepsy foundation improved the efficacy and adherence to the therapies.
SAFETY OF CENOBAmate AS ADJUNCTIVE THERAPY IN ADULTS WITH UNCONTROLLED FOCAL SEIZURES: TIME TO ONSET, DURATION, AND SEVERITY OF THE MOST COMMON ADVERSE EVENTS

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Background and Aims:: Cenobamate is a new antiseizure medication (ASM) approved in the US for uncontrolled partial-onset (focal) seizures in adults. Two international, double-blind, placebo-controlled trials with open-label extensions (OLEs; C013/C017) and a large international open-label safety study (C021) demonstrated efficacy and safety. Here we characterize the most common adverse events (AEs) in these studies.

Methods:: Adults with uncontrolled focal seizures and taking 1-3 concomitant ASMs were enrolled (C013/C017/C021). Concomitant ASM changes were not allowed during the double-blind period (DB) but were allowed during OLEs (C013/C017) and C021. C021 cenobamate titration started lower and uptitrated slower than C013/C017. Time of first onset (pooled C013/C017 DB and OLEs; C021), duration of all AEs (pooled C013/C017 DB), and severity (pooled C013/C017 DB; C021 first 18 weeks) of somnolence, dizziness, and fatigue were examined.

Results:: First onset of the most common AEs emerged throughout both the DB and the OLE, mostly during titration. In C021 the peak occurred when dosing reached ≥50 mg/day. Median duration in days (DB, all occurrences) was: somnolence 32 cenobamate versus 22 placebo, dizziness 11 cenobamate versus 8 placebo, and fatigue 34 cenobamate versus 20.5 placebo. AEs in the DB were primarily mild or moderate, with few severe AEs. In C021, more patients reported mild AEs and fewer reported moderate and severe AEs.

Conclusions:: Onset of the most common AEs occurred primarily during titration and were mainly mild or moderate in severity. The slower titration reduced the severity of AEs.
Background and Aims:: Epilepsy is a common neurological disorder. During the attack, patients may lose their consciousness, body control, and may be injured, hence the prevalence of injuries among patients with epilepsy is high. The aim is to study the prevalence and predictors of SRIs.

Methods:: this was a cross-sectional hospital-based study. A multistage cluster sampling technique. A self-structured questionnaire was used for interviewing the patients

Results:: Among 112 interviewed patients with epilepsy, 49% were male and 51% females. 40% of the patients had a history of SRIs and the most common were head injuries 86%, followed by dental injuries 28%, soft tissue injuries 20%, and fractures 2%. The prevalence of SRIs was high among patients who had a history of status epilepticus 54%, then those on polytherapy 50%, and who were practising high-risk activities 46%. 41% of the patients received nonmedical treatment herbal and spiritual which did not influence the prevalence of SRIs. 69% of the patients interrupted taking their medications due to medications unavailability, freedom of fits, side effects of the drugs, and fasting in Ramadan, respectively. 46 patients discontinued their job/school due to the disease and the prevalence of SRIs among them was 37%.

Conclusions:: the prevalence of SRIs among our patients was high. Factors that increased the frequency of SRIs were; having a history of status epilepticus, being treated by more than one type of medications, treatment interruption, and practising high-risk activities. Nonmedical treatment had no influence. SRIs had a negative impact socially.
EEG SEIZURE ONSET PATTERNS IN STATUS EPILEPTICUS

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Background and Aims: Introduction: The seizure-onset (SOn) patterns have been studied especially with intracranial electrodes to improve the determination of the epileptogenic zone. Qualitative and quantitative EEG studies characterizing the onset pattern in status epilepticus (SE) are lacking. We aimed to classify the different SOn patterns and to compare them in order to determine any possible differences in terms of mortality, morbidity and treatment response.

Methods: Materials and methods: we reviewed retrospectively EEG recorded from adult patients admitted for focal and repetitive SE, from January 2015 to August 2019. In accordance with earlier studies of scalp seizure (Tanaka 2018), we identified 5 patterns of seizure-onset: (1) rhythmic slow activity: sinusoidal activity at <13 Hz; (2) paroxysmal fast activity: sinusoidal activity at ≥13 Hz; (3) repetitive epileptiform discharge (4) suppression of background activity to ≤10 µV; (5) no visible EEG pattern because of artifacts at seizure onset. For each patient from 1 to 5 seizures were analyzed.

Results: 307 seizures were analyzed from 100 patients; the most frequent SOn pattern was the number 3 (39 patients) followed by pattern 1 (34 patients) and pattern 2 (14 patients); pattern 4 and 5 were less frequent (1 and 3 patients respectively). Some patients presented with multiple patterns. Any statistical difference in demographics, etiology, semeiology and treatment response variables was observed; while in term of mortality the SOn pattern 3 showed higher mortality.

Conclusions: studying SOn patterns could improve our understanding on SE mechanism and could become a useful tool in every-day clinical practice.
Background and Aims:: The diagnostic of epilepsy and classifying seizure type are very difficult for the physician because of the relative infrequency of events or occurrences just during certain activities or in unique settings. In that context, smartphones are proposing as an alternative to helping clinicians, patients, and caregivers, to reporting seizures, using videos, etc., to help diagnosis. The purpose of this study is to conduct a systematic review and meta-analysis of applications or smartphone devices related to the diagnosis of epilepsy.

Methods:: A systematic review was performed to evaluate the use of smartphone devices to diagnose epileptic seizures compared with the encephalogram, using the databases of MEDLINE, Scopus, Web of Science, and Embase. We plotted studies estimates of sensitivity and specificity on forest plots and in receiver operating characteristics (ROC). The data were synthesized using a bivariate mixed-effects binary regression modeling framework.

Results:: We included only five studies for analysis that evaluated the use of one specific mobile app (n=2), to record an ECG video, and home video of the epileptic seizure using a smartphone (n=3). We found that the smartphone devices have a sensitivity of 66% (CI95% 44 - 83) and specificity 88% (CI95% 76 – 94) to diagnostic epileptic seizure, with an AUC of 0.86 (CI95% 0.83 – 0.89).
Conclusions: The smartphone devices have a good performance in diagnosis epileptic seizures. However, there need more studies to corroborate the results, especially stratifying for the type of smartphone devices.
SUPER REFRACTORY POST-TRAUMATIC STATUS EPILEPTICUS TREATED WITH COMBINING PERAMPANEL AND KETAMINE

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Background and Aims:: Super refractory status epilepticus (SRSE) is a life-threatening condition with no compelling evidence regarding its best treatment. Ketamine and perampanel have shown, in limited case series, to have respectively a potential role in the management of this condition. The association of these two drugs may have potential synergic effects, but its clinical efficacy is still matter of debate

Methods:: We report a case of post-traumatic SRSE that was successfully treated with a combination of intravenous ketamine and oral perampanel and discuss the potential synergic role of these two anti-epileptic drugs.

Results:: A 23-years-old male was admitted for post-traumatic SE to the intensive care unit. His brain MRI scan revealed microhaemorragic diffuse axonal injury. He was unsuccessfully treated with levetiracetam, phenytoin, valproic acid and lacosamide. Weaning of sedation (midazolam and propofol) always resulted in recurrence of SE. Intravenous methylprednisolone did not exert any beneficial effect. The patient was then treated with intravenous ketamine combined with perampanel through nasogastric tube with dramatic response and SRSE cessation after 39 days of ICU. The patient was discharged to a neurological rehabilitation unit and 5 months after SRSE onset he was discharged home: his neurological and neuropsychological were unremarkable and he remained seizure-free. Glutamatergic transmission is crucial in SRSE and the association of perampanel and ketamine acts on this synaptic pathway by antagonizing both NMDA and non-NMDA glutamate ionotropic receptors.

Conclusions:: Targeting glutamatergic transmission with the association of perampanel and ketamine represents a safe and effective strategy in the treatment of SRSE.
LONG-LASTING MEMORY NO LONGER MEANS FOREVER: RELATIONSHIP BETWEEN ACCELERATED LONG-TERM FORGETTING AND AUTOBIOGRAPHICAL MEMORY DISORDERS AMONGST PATIENTS WITH TEMPORAL LOBE EPILEPSY

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**Background and Aims::** Patients with temporal lobe epilepsy (TLE) have difficulties when they are asked to recall remote autobiographical memory. Also, some patients with epilepsy show accelerated long-term forgetting (ALF) over days or weeks for material demonstrated to have been retained when assessed after typical short-term delays. When remote autobiographical memory has been investigated in patients who show ALF, impairments have been detected in most cases, but the extent to which remote autobiographical memory impairments are explained by early consolidation deficits has not been clarified. The aim of this study is to find a relationship between more remote autobiographical memory impairments and ALF.

**Methods::** We are enrolling patients with late-onset TLE. For the present study, we considered 16 TLE patients and 5 healthy subjects. All the subjects underwent a neuropsychological assessment in order to test rates of forgetting over 1-week delay, and the Levine’s Autobiographical Interview to test autobiographical memory from 5 life periods. The scoring categories of the Interview involved recollection of Internal and External events, and their respective details of time and place, perceptual and semantic aspects, and related emotions.

**Results::** These preliminary results show that on recollection of Internal details we observed a temporal gradient amongst healthy subjects, (more memories recalled in recent decades), while patients who show ALF did not show a temporal gradient. Somehow surprisingly, we did not observe the same trend on External details recalled, with the groups showing the same trend of recollection over life periods.

**Conclusions::** The present study is still enrolling late-onset TLE patients and healthy subjects.
SLEEP-WAKE DISTRIBUTION AND CIRCADIAN PATTERN OF FOCAL SUBCLINICAL SEIZURES

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Background and Aims:: To examine the sleep/wake distribution and 24-h periodicity of focal subclinical seizures (FSS) recorded by 24-hour ambulatory EEG (AEEG) in adult patients affected by focal epilepsy.

Methods:: FSS, defined as ictal electrographic discharges with a temporal-spatial evolution lacking subjective or objective behavioral manifestations, with a duration longer than 6s, documented at AEEG, were retrospectively analyzed. The occurrence of FSS during wakefulness or sleep and within 3-h time blocks through a 24-h cycle (intervals I-VIII) was evaluated.

Results:: A total of 192 FSS (mean duration 29.51±15.36s) from 20 patients (11F,9M, mean age 53.6±20.36y) were studied. FSS occurred more frequently during wakefulness than in sleep (147/192, 76.5% vs 45/192, 23.4%, p=0.02). Mean duration of FSS during wakefulness was comparable to that of FSS during sleep (28.76±15 vs 31.93±16.42s, p=0.25). FSS during interval VII (38/192, 6-9pm) and V (37/192, noon-3pm) were higher than expected. The mean number of FSS during interval III was significantly lower than interval I (0.85±3.34 vs 1.2±3.76, p=0.038) and interval VI (0.85±3.34 vs 1.55±3.94, p=0.010). More patients had FSS in interval VI compared to interval III (11/20 vs 3/20, p=0.039).

Conclusions:: FSS do not occur randomly but follow a specific circadian pattern and a particular sleep-wake distribution. In fact, FSS mainly tend to occur during wakefulness and they have a significant propensity to arise in the time slot 3-6pm, whereas they are less likely seen on awakening. Relevance of FSS arises from the potential effect on cognitive functions and their circadian pattern deserves interest as to a possible chronotherapy.
Background and Aims:: Capgras syndrome is a condition characterized by the belief that a close relative has been replaced by an almost identical imposter. The disorder has long been associated with psychiatric diseases, but it has also been reported in several neurological disorders. In the context of epilepsy, the occurrence of Capgras syndrome has been documented mainly as a postictal or interictal manifestation. We report a case of a focal seizures presenting as transient Capgras syndrome, which, based on existing literature, represents an exceptional manifestation of this syndrome.

Methods:: We describe the case of a 83-year-old woman with focal temporal seizures manifesting as transient Capgras syndrome. The patient abruptly presented with the belief that her husband had been replaced by a nearly identical substitute; the symptoms gradually disappeared within 24 hours. The patient was admitted to our Department to perform further investigation.

Results::
Brain MRI showed the presence of a large right frontobasal meningioma with marked perilesional oedema and mild compressive effect on adjacent structures. Surgical treatment was postponed because of age, comorbidities and patient decision. The patient was started on levetiracetam 500 mg b.i.d. and dexamethasone without seizure recurrence.

**Conclusions:** Our patient represents an exceptional case of Capgras syndrome for several reasons, namely the association with meningioma, very rarely reported before, the transient manifestation of symptoms, and, most importantly, the epileptic etiology of reduplicative paramnesias. Lastly, our report also confirms the importance of frontal and right hemisphere dysfunction in generating Capgras syndrome-like delusions.
Background and Aims:: There is little historical and ethnographic work examining the impact of epilepsy on long-term relationships in Africa. Here, we take a culturally sensitive approach to try and better disentangle factors that may contribute to misconceptions about epilepsy in Zimbabwe.

Methods:: Initially, through a series of community-based workshops organised by the Epilepsy Support Foundation of Zimbabwe, we analysed stigmatisation of epilepsy in urban and rural settings. Workshops consisted of initial presentations on epilepsy followed by small group discussions. We implemented learning from these workshops to develop surveys, translated into native Zimbabwean languages, to capture, at scale, how both the person with epilepsy and those close to them perceive epilepsy.

Results:: Around 100 people participated in workshops based in Harare, Masvingo and Gweru. Considerable stigmatisation persists, particularly perpetuated by older members of local communities. Men with epilepsy felt disempowered by their ability to not work or participate in certain social activities. Both men and women agreed, however, that females with epilepsy were more likely to be subject to prejudice and potentially exposed to greater risk – for example having to cook on open fires away from other village members. While the survey questionnaires are prepared, deployment has not yet proved possible owing to the COVID 19 pandemic.

Conclusions:: Our study again emphasises that multiple misconceptions surround epilepsy, which can lead to severe stigmatisation. The surveys will provide the detailed insight necessary to develop tailored solutions to help empower those with epilepsy as well as the friends and family who help care for them.
SERUM NEUROFILAMENT LIGHT AS A BIOMARKER OF NEURODEGENERATION IN STATUS EPILEPTICUS.

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Background and Aims:: Neurofilaments (Nf) are intermediate filaments specifically expressed in neurons. Nf might be released from damaged or diseased axons in significant amounts into blood and cerebrospinal fluid (CSF) thus, they could be used as potential biomarkers of neurodegeneration. Elevation of serum Neurofilaments Light (sNfL) has been reported in drug resistant epilepsy and in post-anoxic electrographic status epilepticus. The purpose was to evaluate sNfL in patients with Status Epilepticus (SE).

Methods:: We retrospectively measured the serum NfL concentrations of age and sex-matched 30 prospectively collected adults with Status Epilepticus (SE) and compared them with 30 epileptic patients (EP) and 30 healthy controls (HC).

Results:: SE patients have significantly higher sNfL concentrations compared to EP and HC (p < 0.001). In SE patients, sNfL levels have a high correlation with CSF NfL and t-TAU concentrations (τ = 0.68, p < 0.001 and τ = 0.63, p < 0.001 respectively). SE sNfL levels demonstrated a positive correlation with the duration of SE (τ = 0.51, p = 0.003) and were significantly increased in patients with Refractory and Super-Refractory SE (RSE/SRSE, τ = 0.38, p = 0.048). Patients with 30-days worsening of clinical conditions compared to the baseline or death had higher levels of sNfL (τ = 0.38, p = 0.049).

Conclusions:: These exploratory data suggest the role of sNfL levels as a neurodegeneration biomarker in patients with SE. sNfL is a reliable and an easy obtainable biomarker in patients with SE that reflects CSF NfL and t-TAU levels.
CASE REPORT: FAVORABLE RESPONSE TO CARBAMAZEPINE IN SCN1A RELATED EPILEPSY

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Background and Aims:: Sodium Voltage-Gated Channel Alpha Subunit 1 (SCN1A) related epilepsies are known for being a contraindication to sodium blockers antiepileptics under the risk of seizures worsening. We aim to describe the response to carbamazepine (CBZ) at a patient with confirmed Dravet Syndrome.

Methods:: A case report was written with data from medical report of a 25 years-old man, collecting the cronomology that link seizure improvement to CBZ usage.

Results:: The subject had a tonic-clonic seizure after difteria vaccine with 6 months old. He evolved with reflex mioclonic seizures to fever and hot baths. After a status epilepticus (SE) with 4 years old, he presented developmental delay, intellectual disability, autistic features, behaviour disturbance and motor retardation. After SE, he started about fifty focal seizures a day and was unresponsive to several antiepileptic drugs. Carbamazepine (CBZ) was then started at age of 14 and kept due to response at seizure frequency reduction to 2-5 daily episodes, maintained until nowadays. When tried to suspend CBZ there was an epilepsy worsening, controled by reintroduction. The next-generation sequencing at 25 years old was positive for a frameshift SCN1A mutation. MRI at 4 years old showed periventricular nodular heterotopias. The electroencephalogram presented temporoparietal and generalized epileptiform activity.

Conclusions:: Several articles state that carbamazepine is contraindicated at SCN1A epilepsies due to risk of seizure worsening. Genetic polymorphisms of SCN1A could explain the variaty of responses to CBZ. This case shows an unusual response to CBZ to record that sodium blocker antiepileptics are a possible treatment for refractory SCN1A epilepsy.
STATUS EPILEPTICUS: INCIDENCE BEFORE AND DURING THE COVID19 PANDEMIC IN THE PROVINCE OF MODENA, ITALY

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Background and Aims:: Background. Many cardio-cerebrovascular diseases had a lower incidence in the initial phase of the spread of the SARS COV2 virus¹,². Some studies have evaluated the effect of the pandemic on status epilepticus (SE), in particular reporting the absence of significant variations between the cases that occurred before and those during the lockdown, except for the reduction of NCSE³.

Methods:: Methods. We evaluated the incidence of SE cases in the province of Modena, in the 5 months before the pandemic (October 2019-February 2020) compared with the same months of the following year (October 2020-February 2021), during the second and third wave.

Results:: Results. We identified 87 patients with SE in the 10 months analyzed, of which 43 in the pre-COVID19 era and 44 in the COVID19 era. The statistical analysis does not show significant differences between the two groups in terms of age, gender, average length of hospitalization and SE, etiology, semeiology, refractoriness, nor in terms of patient outcome (mRS). Instead, there is a trend in reduction of cases in the COVID19 era that performed EEG within the first 24 hours. There was a significant decrease in cases with in-hospital onset in the COVID19 era (p = 0.009).

Conclusions:: Conclusions. Our data confirm that the pandemic had no significant effect on the incidence of SE. The lower incidence of in-hospital onset SE, as well as the fewer patients with EEG within 24 hours, could indicate a reduced diagnosis of SE and consequently a decrease in SE treatment in the
References


NOCTURNAL ENURESIS AS A SYMPTOM OF IDIOPATHIC PARTIAL EPILEPSY.

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Background and Aims:: During a 6-year prospective follow-up were found 2 cases of a combination of nocturnal enuresis and partial convulsive syndrome in adults.

Methods:: The first patient T., 54 years old, complained of nocturnal enuresis for 3 years, focal seizures of the left arm for 1.5 years. Patient had not suffered from anything before, the beginning of the enuresis was every 2-3 months and became more frequent up to 1 time in 1-2 days. The seizures increased from 1 time in 2 weeks to 1 time in 2-3 days. MRI of the brain: vascular encephalopathy, EEG monitoring for 1 hour: acute-slow wave complexes in the fronto-parietal-temporal regions of both hemispheres of the brain. The second patient is 28 years old, since childhood there is nocturnal enuresis once 3-4 months. For the last 2.5 years, insomnia and continuous, large-sweeping, rhythmic twitching of the left leg have been troubling. The patient was treated for 1 month with a diagnosis of restless legs syndrome, but not effectively. After MRI and EEG monitoring, pathological activity was revealed in both fronto-parietal-temporal regions. No urological pathology was revealed in both patients.

Results:: Patients were diagnosed with focal epilepsy with nocturnal enuresis and given anticonvulsant therapy, with the disappearance of the both symptoms over time.

Conclusions:: Conclusion: Nocturnal enuresis may be a symptom of an epileptic seizure or the only symptom of idiopathic partial epilepsy, which requires further investigation.
PERAMPERAL AS ONLY CONCOMITANT ANTISEIZURE MEDICATION IN PEOPLE WITH EPILEPSY (PEROC STUDY). A REAL WORLD STUDY.

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Background and Aims:: the objective of this study was to assess the dose-related retention rate of Perampanel (PER), as a reliable proxy for overall tolerability and effectiveness, in adolescent and adults who received PER as a part of routine clinical care and as an adjunctive treatment to a previous monotherapy.

Methods:: we performed an observational, retrospective, multicenter study on people aged >=12 years with focal or generalized epilepsy consecutively recruited from 54 Italian epilepsy centers. All patients received PER as the only add-on antiseizure medication (ASM) according to standard clinical practice. Retention rate, seizure frequency and adverse events (AEs) were recorded at 3, 6 and 12 months after PER introduction.

Results:: In detail, 525 patients taking PER with at least 3 month follow-up were collected (215 males, mean age 40 years, SD 20.4). The retention rate at 3, 6 and 12 months follow-up was respectively 87%, 66% and 42%. The 50% responder rate at 3, 6 and 12 months was 66%, 69% and 69%. The seizure free rate at 3, 6 and 12 months was 39%, 59% and 59%.

Conclusions:: these preliminary data confirm the good efficacy of PER for focal or generalized epilepsy in real-life conditions. We provide the first data about its effectiveness as only add-on medication even in patients with a long-standing history of epilepsy and previously treated with many ASMs.
EPILEPSY AND COVID-19: IS INFECTION CORRELATED TO AN INCREASED RISK OF SEIZURE RECURRENCE?

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Background and Aims:: The objective is to study the seizure dynamics in suffering COVID-19 patients with epilepsy, based on clinical observations and analysis of seizure progression.

Methods:: The study design was a single-centre retrospective uncontrolled open-label observational study of the impact of COVID-19 on the course of epilepsy. Suffering COVID-19 patients with epilepsy were interviewed between January and February 2021 using a questionnaire containing three sets of questions.

Results:: The study included 13 suffering COVID-19 patients with epilepsy: genetic (idiopathic) generalised (7/13; 54%), 6 cases of focal epilepsy (6/13; 46%). 2 questionnaires have not been answered yet. The mean age was 34.31±12.68. Seizure remission prior to COVID-19 was noted in 10 patients (77%), there was no seizure control in 3 cases of focal epilepsy at the time of COVID-19 (23%). No seizure frequency increase was observed in any case. No recurrent seizures were detected. EEG follow-up showed no exacerbation of seizures compared to the pre-outbreak indicators. AED monotherapy was used in 61% of cases. Levetiracetam monotherapy administered to 50% of patients and LEV taken as a part of a polytherapy regimen - in 100%.

Conclusions:: The research findings and literature data show that patients with epilepsy are at no greater risk than the general population. Young age, seizure remission, absence of somatic comorbidities, modern drug use with no interaction among AEDs and antibiotics and antivirals for the coronavirus disease treatment can be considered as positive predictive value of the course of epilepsy with COVID-19. Further studies with a large sample sizes are needed.
Background and Aims:: Aim: Cerebrovascular diseases (CVD) and their risk factors are the most frequent serious conditions in neurology that should be prevented. Epilepsy is one of the consequences of these conditions that affect not only elderly, but also younger adults. The aim is to show different vascular etiologies in epilepsy.

Methods:: Among different epilepsy etiologies we selected those with vascular etiologies and evaluated their presence under the umbrella of cerebrovascular etiology for epilepsy. We evaluated the characteristic features of each specific cerebrovascular etiology. 100 patients were selected and evaluated clinically, electrophysiologically, neuropsychologically and with imaging methods.

Results:: The most frequent etiology was stroke and cerebrovascular risk factors: hypercholesterolemia, high blood pressure, diabetes, obesity, smoking, carotid arteries stenosis, atrial fibrillation, lacunar cerebral insults present in 88 mostly elderly people, who were diagnosed with epilepsy with a time delay in some, as their seizures were not recognized at seizure onset, even in cases of nonconvulsive focal epileptic status, because of their comorbidities. Arteriovenous malformation (AVM) as a rare etiology, was present in 7 patients mostly children. Vasculitis as etiology was present in 3 young females with systemic lupus erythematosus. Cerebral venous thrombosis was present in 2 young females during postpartum period.

Conclusions:: Conclusion: Epilepsy is a frequent consequence of CVD and should be timely diagnosed and appropriately treated to prevent further disease burden and disability. Although CVD are typical for elderly, some less frequent CVD appear in young adults and even in children. CVD and their risk factors as etiology for epilepsy should be prevented.
GENDER-SPECIFIC TREATMENT FOR PHARMACORESISTANT EPILEPSY IN NEUROSURGICAL PATIENTS.

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Background and Aims: In the XXI century, the range of antiepileptic drugs (AEDs) has significantly expanded, and gender aspects in AED treatment are urgent. The objective was to investigate gender-specific aspects of AEDs management in neurosurgical patients with pharmacoresistant epilepsy (PhRE).

Methods: In this retrospective study 60 neurosurgical patients with PhRE were examined in two gender groups: 1 - men (N 30) and 2 - women (N 30) at the PNI in 2020. The sex ratio was 1:1. The anamnesis of AED management was evaluated for 3 generations: 1-old and traditional, 2-new, 3-the newer. The frequency of use of AEDs of different generations was calculated on average per patient in the groups.

Results: The use of old AES in group 1 averaged 1.8 per person, more often in the female group - 2.6. New AEDs were used in both groups – 2 per person, newer AEDs were increasingly used in group 1 - 2 per person, 1 - in group 2. Attention was drawn to the percentage prevalence of valproic acid use in both groups compared to the others: in group 1 in 19.3% of cases, in group 2 – in 15.8%.

Conclusions: The use of old-generation drugs in the anamnesis was noted in all patients. The predominance of the use of valproic acid to treat epilepsy in both sexes shows that despite the pronounced side effects affecting the female reproductive system the effectiveness in severe and prolonged epilepsy determines the widespread use of valproates in both men and women despite new drug development.
ROLE OF PEROXISOMAL PROLIFERATOR-ACTIVATED Y-RECEPTORS IN ANALGESIA INDUCED WITH CEREBELLAR STIMULATIONS IN KINDLED RATS

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Background and Aims: Background. Antiepileptic effects induced with cerebellar transcranial direct current stimulation (TDCS), and the role of peroxisomal proliferator-activated y-receptors (PPARγ) in its development have been shown (Godlevsky, Pervak, 2017; 2019). Aims. To investigate the pronouncement of pain behaviors in rats with anodal TDCS of cerebellum and modulation of PPARγ activity.

Methods: Material and methods. Investigations were performed on rats with the kindling induced by pentylenetetrazol (PTZ) injections (30.0 mg/kg i.p., for three weeks). TDCS was performed with anode upon cerebellum (300 mcA for 10 min). BADGE (100.0 mg/kg, i.p.) was used for blockade PPARγ and pioglitazone (100.0 mg/kg, i.p.) for their activation. For the pain test formalin (50 μL; SC; 2%) was injected into either the glabrous skin of the hind limb and the severity of pain reactions was estimated in three points score (Erami, E. et al., 2017). False TDCS was used as a control.

Results: Results. The maximal level of pain behaviors was achieved at 21-27th min from the moment of formalin administration (2.32±0.30 points). TDCS induced a decrease of pain behaviors by 25.7% (P<0.05). After blockading PPARγ with BADGE the pronouncement of pain behaviors was 2.13±0.21 points and after pioglitazone 1.94±0.41 points (P>0.05). TDCS performed after pioglitazone administration caused the decrease of painful behaviors by 43,6% (P<0.05), while after BADGE the diminishment was at 16,3% (P>0.05).

Conclusions: Conclusions. Anodal cerebellar TDCS is effective against the second phase of formalin-induced pain in rats. Analgesic effects of cerebellar anodal TDCS were intensified with the agonist PPAR-gamma receptors administration and abolished with their blockade.
DYNAMICS OF INTERHEMISPHERIC COHERENCE IN CHANGING FUNCTIONAL STATES IN ADULTS WITH LOCALIZATION-RELATED EPILEPSY

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Background and Aims:: Study of the dynamics of interhemispheric coherence in patients with localization-related epilepsy with different responses to anticonvulsants in the physiological state (FS) of active, relaxed wakefulness and sleep.

Methods:: Research methods: 150 patients with symptomatic epilepsy of frontal-temporal localization aged 16 to 65 years with a disease duration of at least 2 years (group A - 78 individuals with a resistant form of the disease, group B - 78 individuals with controlled seizures) were monitored with the EEG in the interictal period in physiological states of wakefulness and physiological sleep in the daytime. Night sleep deprivation was used as a load. For coherent analysis, we used EEG regions devoid of artifacts during the period of relaxed wakefulness, active wakefulness, and during the 2nd-3rd stage of the slow-wave sleep phase immediately before the onset of α-sleep. Hyperventilation load and cognitive activation were used as stress tests in FS AB, which was performed by the method of cognitive evoked potentials P300 using auditory stimuli.

Results:: In groups A and B, there was an increase in interhemispheric coherence in the β-rhythm range during cognitive activation. Group B showed an increase in interhemispheric coherence in the δ-rhythm range during hyperventilation and a decrease in the β-rhythm range during cognitive activation. The dynamics of interhemispheric coherence was observed in the frontal zones, which are most dependent on the coordinating influences of the median structures of the brain.

Conclusions:: In patients with seizures, regardless of frequency, similar neurodynamic rearrangements were observed, manifested by unidirectional dynamics of coherence indicators.
Background and Aims: Seizures are a common manifestation of autoimmune encephalitis (AIE), and in some cases may not respond to antiseizure medications. Epileptogenesis in AIE is likely to arise from the synergistic effect of both innately driven neuroinflammation and antibody-induced hyperexcitability. We describe a case of concurrent anti-AMPAR encephalitis and thymomatous myasthenia with refractory focal status epilepticus.

Methods: Case report

Results: A 64-year-old man, with a thymomatous myasthenia gravis, presented dysautonomia, a 2-month history of memory deficits and mood disturbances. T2/FLAIR hyperintense temporal and frontal bilateral cortical lesions were detected on brain MRI, with hypermetabolism in the same areas on PET-CT. AMPAR Glur2 antibodies were identified in cerebrospinal fluid. The patient manifested prolonged episodes of confusion with inappropriate responses to questions, but he was able to understand simple instructions. EEG showed continuous focal seizure pattern over the left frontal and temporal regions consistent with focal status epilepticus. Intravenous benzodiazepines, levetiracetam, valproate and lacosamide were prescribed with no clinical/EEG improvement. There was a dramatic response to oral perampanel, with complete symptoms and EEG epileptiform abnormalities resolution over 3 days. Treatment with intravenous immunoglobulins, methylprednisolone, plasma exchange and surgical thymectomy was performed, with clinical benefit.

Conclusions: AIE provides a human model of neuroinflammatory epileptogenesis in which two components likely work synergistically. Preclinical studies evidenced AMPAR internalization in anti-AMPAR encephalitis, leading to reduced epileptic threshold. Moreover, Glur1-2 imbalance has been observed in status epilepticus. In our case, perampanel possibly contributed to seizures control by acting as selective and noncompetitive AMPAR antagonist.
TRANSIENT POST Ictal FEVER: AN INFREQUENT SYMPTOM.

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Background and Aims:: Fever is a response to stimuli leading to the deregulation of the central thermostatic control. It is well-known that hyperthermia is a significant seizure-inducing factor, but it is unusual to be observed in the post-ictal period.

Methods:: We present the case of a 41-year-old man, admitted to our Department due to multiple generalized convulsions since the early hours on the day of admission. He had a 20-year history of epileptic seizures, after sustaining head trauma in a car accident. He was taking valproate long-term, with poor adherence, and carbamazepine for 6 months. On admission the patient had full consciousness, and the neurological examination, blood pressure and blood glucose test were normal. His body temperature was 38.8°C.

Results:: An infectious cause of fever was investigated. A complete laboratory and imaging examination (WBC, ESR, CRP, liver biochemical tests, blood and urine cultures, PCR for SARS-CoV-2, CXR) was performed. Tests returned normal or negative, ruling out an infection. Brain CT revealed a porencephalic lesion on the left occipital lobe and signs of a craniotomy on the right temporal side. EEG showed slow theta activity in the left temporo-occipital area. The fever resolved spontaneously in about 12 hours.

Conclusions:: Fever is a well-known seizure-inducing factor, but an infrequent condition in post-ictal period. It is hypothesized that this symptom is a consequence of peri-ictal repetitive muscular contractions and disturbance of homeostasis in generalized convulsive seizures. It also seems possible that the upregulation of the hypothalamic thermoregulatory center can produce it. The investigation for infectious causes is necessary.
EPILEPSY ONSET IN PUBERTY

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Background and Aims:: Purpose: to study onset age and features of onset in puberty at girls with epilepsy

Methods:: Research is part of a prospective observational uncontrolled comparative study of the antiepileptic drugs reproductive side effects. The age of epilepsy onset was studied at 155 female patients older than 16 y.o. Patients were divided into three groups according to WHO classification of puberty age (1997): 1gr. - before puberty- 1-9y.o., 2gr. – puberty- 10-18, 3g. – after puberty- older 18. The frequency of epilepsy onset was studied in 4 subgroups of puberty according to phases of maturing of the hypothalami-hypophysial system: 10-11y.o- beginning of hypothalami-hypophysial hormones secretion, 12-13- beginning menses, 14-15- becoming of an ovulatory peak, 17-18- establishment of a constant rhythm of hormones secretion

Results:: there were 23 patients (15%) in 1 gr., 92 (59%) – in 2gr, 40 (26%) – in 3 gr. Differences in the epilepsy onset in the comparison groups were statistically significant above in puberty (p <0,001). Epilepsy began in childhood (until 18y.o) in 75%. Epilepsy onset in 4 subgroups of puberty period: subgroup 1 — 18 patients (20%), subgroup 2 — 35 (38%), subgroup 3 — 24 (26%), subgroup of 4 — 15 (16%). Prevalence of epilepsy onset in the integrated age range of 12-16y.o. was statistically reliable (p<0,001).

Conclusions:: Thus, hormonal changes during the puberty period provoked epilepsy onset more often. The epilepsy onset occurred more often during the periods of the beginning oestadiol production and its ovulatory peaks (12-16y.o). It confirms proconvulsive effect of estrogens
COVID-19 AND EPILEPSY: DISEASE OR VACCINATION?

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Background and Aims:: to compare the dynamics of epilepsy in patients with COVID-19 disease and the “Sputnik V” COVID-19 vaccination for the prevention of a new coronavirus infection (COVID-19) from a review of two clinical cases.

Methods:: The study design was a single-center retrospective uncontrolled open-label observational study of the impact of COVID-19 on the course of epilepsy. Patients with epilepsy were interviewed during the period January-March 2021 using a questionnaire. Two groups were identified: gr.1 recovered from COVID-19, gr.2 received the Sputnik V COVID-19 vaccine, a measure for COVID-19 prevention. To compare the dynamics of epilepsy we enrolled 1 patient from each group: group 1 patient – with no risk of recurrence after COVID-19 and group 2 patient – with the risk of complicated course of vaccine reactions after neurosurgical treatment for epilepsy.

Results:: Gr.1 included 19 patients who had had COVID-19 and Gr.2 included 2 patients who had been Sputnik V vaccinated for prevention the spread of the novel coronavirus infection. Gr.1 patient, 32 years old, with three-year remission, relapsed with mild COVID-19. Gr.2 patient with focal pharmacoresistant epilepsy with three-year remission after epilepsy surgery had no adverse effects after Sputnik V vaccination, and seizure remission sustained.

Conclusions:: The results of this study showed examples of good tolerability of the Sputnik-V vaccine in an older patient with drug-resistant epilepsy after neurosurgery and the recurrent seizures in younger patients with idiopathic epilepsy and mild COVID-19. The results will help practitioners to decide how to handle an epileptic patient. Further studies with large sample sizes are needed.
Background and Aims:: Epilepsy is a disease associated with myths and taboos, leading to poor understanding and knowledge regarding causes, effects and treatment availability. Public understanding of epilepsy has not been investigated sufficiently so the purpose of this study was to understand the opinions of Accredited Social Health Activist (ASHA) Workers in rural districts of Maharashtra.

Methods:: The survey was conducted before starting an online awareness lecture of the ASHA workers which was organized by Epilepsy Foundation in association with National Health Mission government of Maharashtra. A total of 89 ASHA workers were interviewed, a Marathi questionnaire survey was conducted. The questionnaires contained 15 questions based on Epilepsy and seizures.

Results:: For this study, responses from all included participants (N = 89) were noted. All the participants were divided into 4 regions of Maharashtra, the overall awareness of epilepsy was 58.14%, and the highest awareness was seen in Vidharbha Region and least in Rest of Maharashtra region 67.13% and 53.15% respectively.

Conclusions:: ASHA workers in Maharashtra are not very well acquainted with epilepsy and have many erroneous beliefs about the condition. Negative attitudes are pervasive within communities in Maharashtra. The National Health Mission government of Maharashtra should conduct the awareness programs to clarify the purported modes of transmission of epilepsy, available treatment options and care offered during epileptic seizures during community sensitizations in our settings.
LATE-ONSET EPILEPSY WITH UNKNOWN ETIOLOGY: NEUropsychological profile, CERebrospinal fluid BIOMARKERS, AND QUANTITATIVE EEG CHARACTERISTICS

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Background and Aims:: Despite epilepsy has been associated with cognitive decline, neuropsychological, neurobiological and neurophysiological features in patients with late-onset epilepsy of unknown etiology (LOEU) are still unknown. This cross-sectional study aims at investigating neuropsychological profile, cerebrospinal fluid (CSF) biomarkers of Alzheimer’s disease (AD), and resting-state quantitative electroencephalographic (qEEG) cortical rhythms in LOEU patients with mild cognitive impairment (LOEU-MCI) and with normal cognition (LOEU-CN), compared to non-epileptic MCI (NE-MCI) and cognitively normal (CN) controls.

Methods:: Consecutive patients diagnosed with LOEU-CN (19), LOEU-MCI (27), NE-MCI (21), and CN (11) were enrolled. Patients underwent standardized comprehensive neuropsychological evaluation and CSF core AD biomarkers assessment. Recordings of resting-state eyes-closed electroencephalographic (EEG) rhythms were collected and cortical source estimation with eLORETA was performed.

Results:: Most of LOEU patients had MCI status at seizure onset (59%). Patients with LOEU-MCI performed significantly worse on measures of global cognition, visuo-spatial abilities and executive functions compared to NE-MCI patients (p<0.05). CSF Aβ42 levels were lower in the LOEU-MCI compared with the LOEU-CN group. Finally, parietal and occipital sources of alpha (8-12 Hz) rhythms were less active in the LOEU-MCI than NE-MCI and CN groups, and the opposite was true for frontal and temporal cortical delta sources.

Conclusions:: MCI status was relatively frequent in LOEU patients, involved multiple cognitive domains, and might have been driven by amyloidosis according to CSF biomarkers. LOEU-MCI status was associated with abnormalities in cortical sources of EEG rhythms related to quiet vigilance. Future longitudinal studies should cross-validate our findings and test the predictive value of CSF and EEG variables.
INTERMITTENT LIGHT STIMULATION IN ON-DEMAND STREAMING TELEVISION SERIES, ACCURACY OF INFORMATION AND SEIZURE OCCURRENCE. THE STREAM-LIGHT STUDY.

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Background and Aims:: In about 3% of people with epilepsy (PWE), exposure to flashing light sequences (FLS) can trigger seizures. Exposure to FLS may as well induce other symptoms (i.e. headache and dizziness). On-demand streaming platforms (OSP) have become popular nowadays. Binge watching sessions involve the use of laptops and take place in conditions of low ambient light. The purpose of our study is to identify the presence of FLS in the catalogues offered by the main OSP, and to assess any correlation to seizure or discomfort symptoms recurrence. The presence of adequate information addressed to PWE was evaluated.

Methods:: We carried out a research in online patients’ forums, looking for warnings about FLS reports within TV-series and films offered by the main OSP. Data referred to seizure onset, as well as symptoms of discomfort associated with the vision of a specific show and the presence of adequate warnings, were collected. A re-watch of the TV-series/film by an epileptologist was performed to evaluate the definite presence of FLS.

Results:: 134 TV-series have been identified, with 3334 FLS warnings. Recurrence of seizures was reported in 2 TV-series, 12 were associated with the onset of discomfort symptoms. The platform with the higher number of reports was Netflix. Among all of the analyzed and reported shows, only in one case an FLS information banner was shown.

Conclusions:: The presence of FLS was very frequent in OSP catalogues of films and TV-series. Systematic improvement of information about FLS presence is necessary for greater safety of the audience suffering from epilepsy.
INTERICTAL QTC ABNORMALITIES IN PATIENTS WITH EPILEPSY: EFFECTS OF DISEASE DURATION AND ANTI-SEIZURE MEDICATIONS

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Background and Aims:: Epilepsy is associated with abnormalities in cardiac repolarization as corrected QT interval (QTc) prolongation. The aim of the study is to correlate QTc abnormalities to epilepsy duration and number and class of anti-seizure medications (ASMs).

Methods:: Interictal 12-lead electrocardiograms of 101 people with epilepsy (PWE) without cardiovascular risk factors or chronic diseases were collected. Mann-Whitney or Wilcoxon tests were used to assess QTc differences into PWE dichotomized according to the median value of epilepsy duration and ASMs as appropriates. Correlations between clinical parameters and QTc were assessed using Spearman’s correlation. Variables associated with QTc alterations were tested using logistic regression after dichotomizing QTc according to its median value.

Results:: 101 PWE (47M; 54F) assuming 1 to 3 ASMs were enrolled. Median epilepsy duration was 16 years. QTc median value was 407 msec. Patients with long-standing disease showed increased QTc (p<0.0001) compared to PWE with a shorter epilepsy duration. QTc increased proportionally to the years of disease (Rs:0.429;p<0.0001). No QTc differences were found according to the etiology of epilepsy or seizure type. QTc increased proportionally to the number of ASMs (Rs:0.396; p<.0001) independently from ASM type. Logistic regression confirmed epilepsy duration as the only variable associate to QTc prolongation (p<0.001;HR 4.5).

Conclusions:: Even if the number of ASMs may have a role in QTc alteration, epilepsy duration seems to be the only independent factor causing QTc prolongation.
ADVERSE EFFECT PROFILE OF ANTIÈPILEPTIC DRUGS

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Background and Aims:: L’épilepsie est une maladie neurologique affectant des millions de patients dans le monde. Le traitement par antiépileptiques (AED) est efficace chez environ 70 à 80% des patients, mais il est associé à de nombreux effets indésirables (EI) qui peuvent affecter l’observance des patients.

Methods:: Il concerne une étude transversale chez des patients atteints d’épilepsie (PWE). Un questionnaire a été administré à PWE pour connaître les EI ressentis par eux.

Results:: We included 406 PWE. Among 198 patients on valproate monotherapy, 17.17% developed AEs. Tremor and upset stomach were the most common AEs (4.04% and 3.53% respectively). Weight gain (2.52%), Sleepiness, hair loss (2.02% each), hepatic cytolysis (1.51%) and thrombocytopenia (0.50%) were also reported by our patients. The most frequent AEs reported by patients under carbamazepine were vertigo (7.14), skin rash (5.35), upset stomach (3.57%) and sleepiness (1.78%). Eight patients out of 28 taking phenobarbital presented AEs such as Sleepiness (14.28%) skin rash (7.14%) hepatic cholestasis (3.57%) and shoulder-hand syndrome (3.57%). Among 124 patients on polytherapy, 25 presented AEs (20.16%) which were mainly drowsiness and tremor (7.25%, 4.84% respectively). There was no significant association between AEs, duration of treatment and seizure frequency.

Conclusions:: Drug therapy is the mainstay of treatment of epilepsy. However, AEs often lead to unfavorable quality of life and impaired adherence. That’s why it’s important to examine the tolerability of AEDs.
EFFICACY AND TOLERABILITY OF ANTI-SEIZURE DRUGS IN THE TREATMENT AND PROPHYLAXIS OF BRAIN TUMOR RELATED-EPILEPSY (BRTE): A REAL-WORLD STUDY

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Background and Aims: Brain tumour related-epilepsy (BRTE) is a condition characterized by the development of seizures in the context of a brain tumour pathology. In 40% of cases, seizures represent one of the onset symptoms of brain tumour. According to some studies, the high incidence of BRTE in patients with brain tumour would justify the use of a prophylactic anti-seizure therapy (EST) which in turn would not lead to major side effects (SE). However, such studies do not make an appropriate assessment of neuropsychiatric SE of anti-seizure therapy.

Methods: Thirty-two patients with brain tumour were consecutively selected and divided into two groups: patients with BRTE on AST (BRTE group) and patients with brain tumour on prophylactic AST (PROPHYLAXIS group). Neuropsychiatric SE of anti-seizure therapy were assessed using the Neuropsychiatric Inventory Questionnaire (NPI-Q) at the baseline visit and at 6-month follow-up. The evaluation of the efficacy of the anti-seizure treatment in subjects with BRTE was evaluated according to the percentage reduction in the frequency of seizures at 6 months.

Results: 17 patients in the BRTE group and 15 patients in the PROPHYLAXIS group were included. The drug most commonly used in the two groups was Levetiracetam. The mean scores obtained on the NPI were significantly higher in the PROPHYLAXIS group (p <0.05) as were the scores on the depression (p <0.02), motor activity (p <0.03) and sleep disturbances (p <0.05).

Conclusions: Prophylactic treatment with anti-seizure medication in the context of brain tumour can have a deleterious effect on the psychiatric sphere.
EFFECT OF COVID-19 PANDEMIC ON PEOPLE WITH EPILEPSY (PWE): EXPERIENCE FROM A TERRITORY CARE CENTRE FROM INDIA

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Background and Aims:: Background-Epilepsy if one of the most common neurological disorder and in around 30-40% people with epilepsy sz are refractory. Among different causes (age of onset, aetiology, sz frequency) of breakthrough seizure non compliance to AED and missed dosage is the most common, followed by sleep deprivation and stress. During nationwide lockdown due to COVID-19 pandemic routine OPD services are stopped in most of the medical facilities and only emergency services are on run. AIM-To study the effect of COVID-19 pandemic and different measures taken by authority to contain the pandemic on people with epilepsy (PWE).

Methods:: A cross sectional observational study based on telephonic survey consisting of 15 questions addressing seizure control and reasons behind any change in seizure frequency was conducted in a group of PWE in India in May 2020.

Results:: 211 PWE participated in the interview. Sixteen (7.6%) reported an increase in seizure frequency of which 5 (31.25%, p<.001) were due to unavailability of anti-seizure medications (ASMs). Number of ASMs and time since the last visit to epilepsy clinic was not associated with increased seizure. ASMs were not available to 7 (3.3%), available with difficulty to 45 (21.3%) and freely available to 159 (75.3%) PWE. None of the PWE had COVID-19 infection and none with increased seizure frequency had any symptoms suggestive of COVID-19 infection.

Conclusions:: There is no predisposition to COVID-19 infection or increased seizure frequency due to symptoms suggestive of COVID-19 in PWE in this cohort. Unavailability of ASMs is the most important cause of increased seizure frequency during COVID-19 pandemic for which necessary steps should be undertaken.
Background and Aims:: Multiple sclerosis (MS) is a chronic autoimmune demyelinating disease of the central nervous system. Epilepsy is three times more frequent in patients with MS when compared to the general population. Focal and focal-to-bilateral seizures are the most frequent ones although they can be misdiagnosed as paroxysmal demyelination events causing a delay in diagnosis and treatment. This study aims to investigate clinical, radiological, electrophysiological and neuropsychological aspects between epileptic MS patients and non epileptic MS patients.

Methods:: Twenty-five MS patients with epilepsy (EPI+ group) and 25 age-and-sex-matched MS patients (EPI− group) were retrospectively selected from the database of the Multiple Sclerosis Center at the “SS. Annunziata” Hospital in Chieti. Patients underwent a comprehensive clinical assessment consisting of neurological examination, electroencephalogram (EEG), MRI and neuropsychological testing via the BICAMS (Brief International Cognitive Assessment for MS) - a set of 3 tests to assess cognitive domains: Information elaboration speed (SDMT), Verbal Memory (CVLT-II), Visuospatial memory (BVMT-R).

Results:: EPI+ group showed a significantly higher EDSS, a higher amount of cortical and juxtacortical T2+ lesions and performed worse in SDMT and BVMT-R, compared to the control group. Interictal EEG recording showed interictal epileptiform abnormalities in 13/25 patients in EPI+ group compared to 0/25 in EPI− group.

Conclusions:: Epilepsy causes an important increase in disability (EDSS) and worse neuropsychological score in MS patients suggesting the need for earlier diagnosis and precocious treatment. Interictal EEG recording may help clinician in diagnosis although the limitation due to its sensibility.
Background and Aims:: Poor adherence to medication is common especially in the case of chronic diseases like Epilepsy. Treatment satisfaction may impact adherence. The aim of this study was to measure medication adherence and its relationship to treatment satisfaction, duration of illness and Epilepsy control and to determine the causes of nonadherence in Sudanese patients with epilepsy.

Methods:: This cross-sectional study was conducted in Daoud Charity Clinic. A total coverage of patients with epilepsy fulfilling the inclusion criteria during a period of eight weeks was done. Patients were interviewed and assessed using Hill-Bone medication adherence scale (HB-MAS) and treatment satisfaction questionnaire for medication (TSQM) to measure medication adherence and treatment satisfaction.

Results:: 72 patients were studied. 43% were males and 57% were females. Mean age was 31.28 ± 11.46. Mean HB-MAS score was 34 ± 2.1 indicating high adherence. Adherence was not significantly correlated with duration of illness and there was no significant difference in mean HB-MAS score between patients with well and poorly-controlled epilepsy. 57% reported to have missed their medication more than once because of short supply. Mean treatment satisfaction scores regarding four domains of effectiveness, side effects, convenience and global satisfaction were 84.5 ± 17.7, 92.4 ± 17.1, 83.9 ± 12.8 and 83.4 ± 18.8 respectively. There was a significant correlation between adherence and the convenience domain (p = 0.002), but not the other domains.

Conclusions:: In our sample medication adherence and treatment satisfaction was found to be high in patients with epilepsy. Treatment satisfaction in regard to convenience was significantly correlated to medication adherence.
MEDICATION ADHERENCE IN PEOPLE WITH EPILEPSY

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Background and Aims:: Medication adherence in people with epilepsy (PWE) is a crucial factor to reduce risk of seizure recurrence. Adherence to antiepileptic drugs (AED) increases PWE survival and quality of life, whereas non-adherence is associated with increased mortality and increased hospitalization. The MMAS-8 (Modified Morisky Adherence Scale-8) is a valid instrument to evaluate medication adherence in PWE. The aim of our study is to assess clinical and demographic factors that influence medication adherence in PWE.

Methods:: A population of 118 PWE was asked to answer online questionnaires, with particular attention to: MMAS8, QoLIE (Quality of Life in Epilepsy Inventory), BDI-II (Beck Depression Inventory), GAD (Generalized Anxiety Disorder) e Resilience. We used ANOVA test and Pearson correlation to define the relationship between medication adherence and demographic data, clinical variables (seizure frequency, number of AED) and individual features (quality of life, depression, anxiety and resilience).

Results:: We found that women were more adherent to therapy than men (p<0.01). Duration of illness was positively related to medication adherence. No significant correlation was found between medication adherence and number of AED (p=0.9). Adherence was significantly correlated with depression (BDI-II) and resilience (p<0.05). We found that people with higher scores of BDI-II (moderate and severe depression) were less adherent to therapy. People with higher scores of resilience were more adherent to AED therapy.

Conclusions:: In our study we confirmed that sex, duration of illness and depression are significantly related to medication adherence in PWE. For the first time, we demonstrated that higher resilience is associated with a better medication adherence.
Background and Aims:: Idiopathic generalized epilepsies (IGE) are syndromes diagnosed by clinical and electroencephalographic features. There are four syndromes recognized by the International League Against Epilepsy including childhood absence epilepsy (CAE); juvenile absence epilepsy (JAE); juvenile myoclonic epilepsy (JME); and epilepsy with generalized tonic–clonic seizures only (EGTCS). In the current study, we tried to determine distinctive features to distinguish these syndromes from one another.

Methods:: We conducted a cross-sectional retrospective study over a period of 3 years (2017-2019). We included all patients aged more than 18 years old, with a clinical diagnosis of IGE. We studied the demographic, clinical and electroencephalogram (EEG) findings in all IGE syndromes.

Results:: During the study period, 127 patients were diagnosed as having IGEs (EGTCS: 100, JME: 22; CAE: 3 JAE: 2). The age of seizure onset was 17.83±9.8 years. Epilepsy risk factors were reported to be as follows: parental consanguinity in 49 patients (38.58%), having family history of epilepsy in 40 (31.49%), febrile convulsion in 25 (19.68%). The sex ratio was significantly different in patients with JME compared to EGTCS. The male to female ratio was 0.69 in patients with JME. Interictal EEG was more frequently pathologic in patients with JME compared to EGTCS (P=0.036). In addition, generalized spike-wave complexes were more frequently reported in patients with JME (P=0.0001). Photoparoxysmal response was more frequently observed in patients with JME (P=0.023).

Conclusions:: IGE are common epilepsy syndromes. Additional epidemiological and genetic studies can be useful to better understand clinical and electrophysiological characteristics.
EPILEPSY AND STIGMATIZATION

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Background and Aims:: Epilepsy is a common neurological condition. Stigma associated with epilepsy is common in many cultures. It has a negative influence on the lives of people with epilepsy (PWE) and it contribute to poor outcomes such as isolation, unemployment, lower prospects of marriage and not seeking treatment.

Methods:: We conducted a cross-sectional study of epileptics patients aged 18 to 59, who were followed up at neurological department over a 3-year period. (2017-2019). Demographic (age, gender, marital status, level of education, employment status) and clinical characteristics of the patients were recorded.

Results:: We included 518 people with epilepsy. The average age was 37.34 years (18 - 59 years). The sex ratio was 1.4 (303 M / 215 F). Most of our patients were single (49.4%). Regarding the type of seizure 56.8% had generalized epileptic seizures. Only 34.9% of our patients had a high school or university education level. At the time of the study, only 37.5% had a job. The factors associated with non-professional integration were generalized epilepsy (p = 0.001) and poor response to antiepileptic treatment (0.009).

Conclusions:: Epilepsy is a stigmatizing condition and this facet is rarely studied. Higher unemployment and lower marriage rates indicate that PWE suffer from social problems. Understanding this aspect of epilepsy is important for reducing the burden of epilepsy.
EFFECTS OF THE NONCOMPETITIVE AMPA RECEPTOR ANTAGONIST PERAMPANEL ON THALAMO-CORTICAL EXCITABILITY: A STUDY OF HIGH-FREQUENCY OSCILLATIONS IN SOMATOSENSORY EVOKED POTENTIALS

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Background and Aims:: We designed a longitudinal cohort study on People with Epilepsy (PwE) with the aim of assessing the effect of Perampanel (PER) on cortico-subcortical networks, as measured by high-frequency oscillations of somatosensory evoked potentials (SEP-HFOs). SEP-HFOs measure the excitability of both thalamocortical projections (early HFOs) and intracortical GABAergic synapses (late HFOs), thus they could be used to study the anti-glutamatergic action of PER, a selective antagonist of the AMPA receptor.

Methods:: 15 PwE eligible for PER add-on therapy, were enrolled prospectively. Subjects underwent SEPs recording from the dominant hand at two times: PwET0 (baseline, before PER titration) and PwET1 (therapeutic dose of 4 mg). HFOs were obtained by filtering N20 scalp response in the 400-800Hz range. Patients were compared with a normative population of 15 healthy controls (HC) matched for age and sex.

Results:: We found a significant reduction of Total HFOs and mostly early HFOs area between PwET0 and PwET1 (p=0.05 and p=0.045 respectively) and between HC and PwET1 (p=0.01). Furthermore, we found a significant reduction of P24/N24 Amplitude between PwET0 and HC and between PwET0 and PwET1 (p=0.006 and p=0.032, respectively).

Conclusions:: Introduction of PER as add-on therapy reduced the area of total HFOs, acting mainly on the early burst, related to thalamo-cortical pathways. Furthermore P24/N24 amplitude, which seems to reflect a form of corticosubcortical integration, resulted increased in PwE at T0 and normalized at T1. Our findings suggest that PER acts on cortico-subcortical excitability. This could explain the broad spectrum of PER and its success in forms of epilepsy characterized by thalamo-cortical hyperexcitability.
DEVELOPMENT AND USE OF AN INSTRUMENT (EKAT) FOR ASSESSMENT OF COMPETENCE OF MEDICAL TRAINEES IN PROVIDING EPILEPSY CARE AT VARYING LEVELS OF THEIR TRAINING

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Background and Aims:: BACKGROUND Epilepsy treatment gap in India and many other low and middle income countries can in large part be narrowed if competence to provide non-specialist (primary and secondary) epilepsy care is developed amongst medical trainees at the graduate, postgraduate and super-speciality levels. AIM To develop an instrument and use it for assessing the competence of medical trainees in providing epilepsy care at various levels of training.

Methods:: METHODS The questionnaire based instrument- EKAT (Epilepsy knowledge assessment tool) was developed with the help of epilepsy experts using the Delphi method. It was applied on a small pilot population to calculate its psychometric properties. A cut-off pass score was established using Modified Angoff method. It was then used to assess the competence of 360 medical trainees.

Results:: RESULTS The final version of EKAT was found to have very good internal consistency (Cronbach’s alpha - 0.84), item difficulty range of 11%-87% and good expert inter-rater reliability (ICC - 0.82). The assessment of 360 medical trainees showed statistically significant difference in mean scores and pass percentage across the pre-specified groups: Undergraduates (20.43 ± 7.68, 15%), Interns (23.85 ± 6.0, 20%), Postgraduates (27.57 ± 5.48, 43%), Neurology (34.82 ± 4.43, 97%) and Neurosurgery (26.73 ± 4.73, 32%) with a p-value of < 0.001. Intra-group comparisons and performance in pre-specified domains and levels of proficiency across all groups showed significant differences.

Conclusions:: CONCLUSIONS EKAT is a reliable and valid instrument to assess the competence of medical trainees in epilepsy care across varying levels of proficiency, specialty and training.
BE CAREFUL, ORAL PHENYTOIN CAN CAUSE SINUS ARREST

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Background and Aims:: Phenytoin(PHT) is widely used because of its efficacy in controlling seizures, easy availability and low cos. PHT may occasionally result in cardiac toxicity even death following IV infusion. We report a case of sinus arrest leading to bradycardia on oral treatment. We report this case highlighting cardiac toxicity even on oral treatment with PHT

Methods:: 42 y gentleman presented with new onset left focal seizures with secondary generalization due to arteriovenous malformation which was treated with glue embolization. He was prescribed PHT for focal seizures. Following breakthrough seizures 4y later, PHT dose was increased to 400 mg following which he developed acute onset distension of abdomen, dyspnea and unconsciousness. The patient was afebrile, his pulse was 32/min, BP 90/60 mmHg, respiratory rate 24/min oxygen saturation 55% on room air. His ECG showed bradycardia with atrial escape bigeminy secondary to sinus arrest. He was treated with inj atropine 0.6 mgSC and isoprenaline 5mcg/min. PHT was replaced by levetiracetam 500mg and carbamazepine 200mg twice daily. His pulse increased to 56/min. His white cell counts, blood glucose were normal, serum urea 67mg/dl, creatinine 1.1mg/dL, serum Na 133.0,K 4.8, Ca 8.5, Mg 1.8, PH 7.3 , T3 47.7, T4 6.9, TSH 1.2, serum cortisol 12.9mcg/dl, alkaline phosphatase 124KA, bilirubin 0.8/0.34 mg/dl, SGPT 290.0U/L, SGOT 795.0U/L. His serum phenytoin level done next day morning was 18.0 mcg /ml.

Results:: As he improved, isoprenaline was tapered and he was discharged on 3rd day of hospitalization.

Conclusions:: Serious sinus arrest can occur even on oral PHT
EPILEPSY AND SLEEP DISORDERS: A COMPLEX INTERPLAY

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Background and Aims:: The interaction between sleep and epilepsy is reciprocal, with patients having sleep disorders that are frequently related to the severity of the disease. These disorders are underdiagnosed. They could affect the quality of life of people with epilepsy. We purpose to determine the prevalence of sleep disorders in patients with epilepsy and to evaluate their impact on the quality of life of these patients.

Methods:: This cross-sectional prospective study was carried on patients with epilepsy attending the Neurology outpatient department at Habib Bourguiba Hospital Sfax-Tunisia during 1 month. Data were collected in a questionnaire containing socio-demographic and clinical data. Sleep disorders was assessed using Epworth Sleepiness Scale and Athens Insomnia Scale. Quality of life was assessed using QOLIE-31.

Results:: 33 patients were included of whom 22 were males and 11 were females. 64% of patients had generalized seizures. Insomnia was observed in 78.8% of patients and daytime sleepiness in 45.5% of cases. No correlation was found between sex and insomnia or with daytime hypersomnolence (p = 0.19 and 0.24 respectively). Generalized seizures were associated with a higher frequency of sleep disturbances (p = 0.02). Prevalence of sleep disorders wasn’t affected by anti-epileptic drug. However, daytime sleepiness was correlated with polytherapy (p=0.04). A negative correlation between "emotional well-being" and day time hypersomnolence was noted (p = 0.03).

Conclusions:: Sleep disorders are frequent in our study in accordance with literature data. Hence the importance of a careful evaluation in order to detect and treat them.
NEURAL CD40 MODULATES NEURONAL NETWORK DURING SEIZURES

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Background and Aims:: Unregulated neuroinflammation mediates initiation and maintenance of seizures by inducing neuronal hyper-excitability, interneuron damage, and aberrant post-synaptic formation. CD40L, a small protein belonging to the TNF superfamily that interacts with the CD40 receptor protein, transduces molecular signaling that mediates neurite organization during brain development. The goal of this research was to determine whether CD40 modulates seizure.

Methods:: Adult male CD40 deficient mice (CD40KO) and its respective wild type were used in this study. To evaluate seizure susceptibility successive 35 mg/kg, intraperitoneal (i.p.) doses of pentylenetetrazole (PTZ) given at 5 min up to 6 doses and to test seizure severity PTZ (75mg/kg, ip) was given as single doses. Using a chronically implanted silicon probe in the cortex-hippocampal axis in a group of mice simultaneously, local field potential (LFP) were evaluated during spontaneously behavior and PTZ induced seizures. Seizures severity were evaluated using Racine’s score, including the latency to elicit seizure after PTZ. Frequency analysis from LFP including individual neuronal activity were analyzed using a signal analysis software. Then brain samples were collected to evaluate activation of CD40 and neuronal damage using immunohistology from hippocampal and neocortex.

Results:: CD40KO demonstrated reduction in seizure severity (CD40KO: 0.1± 0.14 S.E.M. vs., WT: 2.8 ± 0.54 S.E.M.; p=0.0003) and in latency compared to WT (CD40KO: 4.45 minutes ± 0.51 S.E.M vs., WT:1.09 minutes ± 0.005 S.E.M. p=0.0008). CD40 reduced seizure induced gamma activity in hippocampal region.

Conclusions:: These preliminary findings indicate that up-regulation of CD40L-CD40 could mediate ictogenesis by influencing inflammatory mechanisms that involve and propagate seizure-induced neuronal damage.
DIFFERENCES IN VISUAL INFORMATION PROCESSING BETWEEN IDIOPATHIC GENERALIZED EPILEPSY WITH AND WITHOUT PHOTOSENSITIVITY

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Background and Aims:: Recently, altered visual cortical processes namely lack of habituation to visual evoked potentials, has been highlighted in both Photosensitive Epilepsy and in a specific i.e. analytic mode of processing visual inputs. In this study we aimed at evaluating the relationship between Photosensitivity and Analytic Style of processing visual information, in a sample of 30 IGE patients and matched Healthy controls.

Methods:: At our Epilepsy unit of the Sapienza University of Rome, we consecutively enrolled 15 IGE patients with Photosensitivity and matched them with 15 IGE patients without Photosensitivity and 15 Healthy Volunteers. All patients underwent EEG recording in basal conditions during hyperventilation (3 Min), and intermittent light stimulation. The instruments used to gather psychological cognitive behavioral data consisted of participation in two tests: the Sternberg -Wagner Self-Assessment inventory and Mariani Learning Style Questionnaire

Results:: In the Visual Style, scores of the photosensitive IGE individuals were significantly higher than the non-photosensitive IGE individuals (p<0.0001,Tukey'post hoc test).

Conclusions:: We discuss these data in the light of our previous evidence highlighting a link between analytic information processing style and altered neurotransmission in other neurological diseases such as primary headaches [. In conclusion an association between Analytic Style of processing visual information and Photosensitivity in IGE has been shown . The common neurophysiological features between these two factors, suggest the possibility to evaluate this cognitive behavior as a potential target for non pharmacological therapeutic strategies in Photosensitive Epilepsy.
CLINICAL FEATURES AND LONGTERM OUTCOME OF RECURRENT STATUS EPILEPTICUS: DATA FROM THE ADULT STATUS EPILEPTICUS POPULATION OF MODENA, NORTHERN ITALY

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Background and Aims:: Little is known about Status Epilepticus (SE) recurrence. We evaluated the clinical features and the longterm outcome of patients with recurrent SE and assessed the risk of recurrence after an incident event.

Methods:: We reviewed our prospective register of consecutive SE episodes of adult patients admitted to the OCB hospital (Modena, Italy), from September 1st 2013 to September 1st 2020. We performed a comparison between recurrent (rSE) and incident SE (iSE) and evaluated the risk of recurrence through a survival analysis. Post-anoxic events were excluded as well as those patients with a SE prior the study period.

Results:: 478 patients were observed. 44 patients (mean age: 67 y/o, 69% female) experienced SE recurrence, whereas 434 patients (mean age: 71 y/o, 61% female) presented an incident event. Among demographic and clinical variables, an acute symptomatic etiology was less frequently observed in relapsing patients (p<0.01), without differences in terms of previously known epilepsy (p=0.53). The highest risk of recurrence was observed in the first 6 months following the incident SE (7.6%), whereas the cumulative recurrence rate in our population was 1.5%, 9.1%, 12.8%, and 15.8% at 30-days, 6 months, 1 year, and 3-years respectively. Comparing iSE and rSE, we did not find any differences in terms of longterm survival (p=0.62).

Conclusions:: SE recurrence was less frequently observed after an acute symptomatic incident event, it was often experienced during the first 6 months of follow-up and apparently did not influence longterm survival in our cohort.
GELASTIC SEIZURES: GOING AFTER THE CAUSE OF LAUGHTER—A SERIES OF SEVEN CASES

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Background and Aims:: Gelastic seizures are epileptic fits of laughter without emotion or joy. These are rare seizure types and particularly related to hypothalamic hamartomas. Neocortical origin is rare but are reported to originate from pathologies in frontal, temporal, and parietal cortex. The aim of the study was to evaluate patients with history of gelastic seizure and Surgical/medical outcome.

Methods:: Detailed birth developmental history along with history of puberty, seizure semiology of other types was obtained in patients with history of gelastic seizure. They underwent 3T MRI with special focus on hypothalamus and long term VEEG and other investigations as required. Surgical/medical outcomes were studied.

Results:: A total of 7 cases (5 male 2 female) with age of presentation from early second to mid of third decade was studied. The etiology consisted of hypothalamic hamartoma in four patients with seizure freedom of Engel class 1 post surgery in three patients. There was recurrence of lesion in one with seizure freedom with drugs and post revision surgery. A young male with focal unaware seizures besides gelastic seizure had right bulky amygdaloid hippocampal formation with uncal and entorhinal cortex FCD but with occipital discharges. A 12-year male with DRE had a history of HIE with developmental delay with focal unaware seizure, GTCS with bilateral perirolandicfrontoparietal gliosis on imaging. A 16-year male with focal unaware seizures, GTCS with normal imaging and generalized discharges with DRE.

Conclusions:: Gelastic seizures in hypothalamic hamartomas have a good surgical outcome. Gelastic seizure can also occur with other etiologies, and have multiple seizure types and DRE.
STATUS EPILEPTICUS AMAUROTICUS IN A PATIENT WITH FAMILIAL PHOTOSENSITIVE OCCIPITAL EPILEPSY

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Background and Aims:: To report the electro-clinical and imaging features of status epilepticus (SE) amauroticus in a patient with subsequent resolution of MR abnormalities and visual deficits.

Methods:: the patient is an 18-year-old-man with photosensitive occipital epilepsy (pOE) that started at the age of 10, with relatively good seizure control, on therapy with valproate and topiramate. His 29-year-old brother had pOE evolving into genetic generalized epilepsy with absences and eyelid myoclonia. His 20-year-old sister also had pOE that spontaneously remitted from the age of 12 years. The proband was referred to our outpatient clinic since he had become complete blindness in the last 10 days without any evidence of other seizures.

Results:: neurological examination revealed complete blindness. EEG revealed sub-continuous focal epileptiform discharges over both occipital lobes. Brain 3T-MRI showed bilateral cortical parieto-occipital hyperintensities in DWI, T2 and FLAIR sequences. Subcortical white matter was relatively spared. Extensive laboratory investigation and cerebrospinal fluid analysis including autoimmune and infectious screening, serum lactate levels, antibodies against cell surface and intracellular neuronal antigens, were all unremarkable. The electroclinical findings fulfilled the criteria of SE amauroticus. Intravenous therapy with levetiracetam and methylprednisolone prompted the disappearance of SE on EEG, with complete resolution of MR abnormalities and visual deficits in a week.

Conclusions:: SE amauroticus represents a rare cause of potentially reversible blindness and should be considered in patients with acute visual loss and a history of epilepsy. It remains to be elucidated the etiopathogenetic mechanism underlying SE amauroticus as also the pathophysiology of reversible MRI alterations, alongside with the underlying genetic factors.
DNA METHYLATION SCREENING SUGGESTS BRAIN ORIGIN OF CELL-FREE DNA IN EPILEPSY

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Background and Aims:: Cell-free DNA (cfDNA) are small circulating DNA fragments generally defined as cellular death debris. The profiling of the cfDNA methylome has been successfully used to track the origin of these circulating nucleic acids, which greatly upgraded the clinical applicability of liquid biopsies. The prediction of tissue specific cell death may represent a valuable tool in early disease diagnose and identification of undetermined pathology. The main histopathological feature of Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis (MTLE-HS) is severe neuronal death in the mesial regions. Increased cfDNA total levels have been previously reported in MTLE-HS, although the potentially cerebral origin is still undisclosed.

Methods:: We performed DNA methylation profiling, using Infinium MethylationEPIC BeachChips, in cfDNA isolated from serum of seven MTLE-HS patients (3M, 4F; 45.3±9.7 years of age) and seven non-epileptic controls (1M, 6F; 43.3±5.1 years of age). The meth_atlas algorithm, encompassing 25 specific cell and tissue types, was used to deconvolute cfDNA origin. Methylation array data processing and differential methylation was performed with the R statistical language.

Results:: A slight increase in the proportion of “cortical neuron”-derived cfDNA was observed in MTLE-HS patients. We identified 107 CpG positions differentially methylated between patients and controls. Gene ontology analysis revealed striking enrichment of terms associated with cerebral cortex GABAergic neuronal pathways.

Conclusions:: We demonstrate for the first time the presence of cfDNA derived from cerebral tissue in MTLE-HS patients. DNA methylation profiling of cfDNA in MTLE-HS can present major utility as early diagnostic or predicative biomarkers of hippocampal sclerosis.
MULTIPLE DRUG INTERACTIONS INDUCED HYPERAMMONEMIC ENCEPHALOPATHY IN DRAVET SYNDROME

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Background and Aims:: Metabolic encephalopathy is a rare and serious complication of some antiseizure medications (ASMs). Stiripentol (STP), valproic acid (VPA), and topiramate (TPM), alone or in combination, may facilitate this condition. Possible mechanisms for this drug-associated/drug-induced toxicity are debated.

Methods:: Case Report

Results:: A 28-year-old girl with Dravet Syndrome was treated with several ASMs, including a combination of STP, VPA, clonazepam, and TPM that determined a subtle management of seizures. After a month from the beginning of TPM she presented gait ataxia, dizziness, and drowsiness. Video-EEG revealed diffuse slow delta activity with isolated epileptic discharges in the frontal regions. Serum VPA and TPM levels were maintained within the therapeutic range. Liver function was normal. However, the serum ammonia level was elevated, over 10 times the normal range (1509ug/dL). Given the pharmacokinetic and pharmacodynamic interactions, especially between VPA and TPM, the latter was suspended. The patient also received lactulose, branched-chain amino acids and low protein diet. After several days, the serum ammonia level was back to normal, EEG showed no pathological activity, and the patient recovered the quo ante status. Brivaracetam has been introduced to achieve a better control of seizures, but has been rapidly discontinued for lack of response. Afterwards, cannabidiol was introduced with mild improvement of clinical behaviour and seizure control.

Conclusions:: Polypharmacotherapy raises the risk of drug interactions and severe side effects in patients with epileptic encephalopathy. Early diagnosis of hyperammonaemia is essential to reduce neurological consequences and TPM should be used carefully in patients receiving VPA or STP therapy.
AWARENESS OF DRIVING REGULATIONS AMONGST PERSON WITH EPILEPSY AND THEIR CAREGIVERS

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Background and Aims:: In India persons with epilepsy (PWE) are prohibited to drive by the law (The Motor Vehicles Act 1939). Though there can be hazardous consequences of a road accident like head injury, awareness about the same is poor amongst the PWE, caregivers and the public. The aim of the study was to assess the awareness of PWE and caregivers about the driving regulations in India and the consequence of driving by PWE.

Methods:: The study was conducted in a tertiary care center in Northern India; Institute Ethics Committee approved the protocol. All PWE (≥ 18 years) and their caregivers were asked to fill a pre-structured questionnaire assessing the awareness about driving and responses were analyzed.

Results:: A total of 196 PWE and 113 caregivers filled the questionnaire. Median age of PWE was 27 years (range 18-65 years); 64% were females. While 94.4% PWE understood about the implications of driving, only 14% were aware about the driving prohibitions by the law. About half of the PWE (54%) were explained about the hazards of driving by their physicians and were asked not to drive. Among the caregivers 43.4% were aware of the law prohibiting driving; 76% felt that driving by PWE is hazardous and 70% thought that PWE should refrain from driving.

Conclusions:: There is considerable lack of awareness about the driving regulations and consequences of driving in PWE; educating the PWE, caregivers and public about the same will help to prevent the road accidents. Funding Source: ICMR, New Delhi, India
UTILITY OF 8-CHANNEL EEG IN DETECTING INTERICTAL GENERALISED SPIKE AND WAVE DISCHARGES - A DIAGNOSTIC STUDY

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Background and Aims:: The EEG can be valuable in the diagnosis of generalized epilepsies. In low and middle-income countries, expertise in reading EEGs is extremely limited and inaccessible for most. EEGs with fewer channels are both easier to perform and read. Non-specialists can be trained to read 8-channel EEGs. We therefore tried to determine sensitivity of 8-channel EEG in detecting interictal GSWDs as compared to 21 channel EEG.

Methods:: In this study EEGs were reviewed by two independent reviewers R1 and R2 using both 8 and 21 channels. The sensitivity and specificity of 8-channel EEG was assessed considering 21-channel [R1] as gold standard. EEGs were reviewed randomly in 8 and 21 channels according to a pre-decided protocol. Background, GSWDs, focal discharges and localisation, focal slowing and localisation were reported.

Results:: A total of 1876 EEGs were evaluated. Of 169 EEGs showing GSWDs in 21-channel, 9 (5.3%) were missed in the 8-channel EEG, while 5 EEGs with GSWDs reported on the 8-channel EEG were not picked on 21-channel. In detecting GSWDs 8-channel EEG has positive predictive value of 97% (95% CI 93.1-99.0%) and negative predictive value of 99.5% (95% CI 99.0-99.8%). The sensitivity of 8 channel EEG in detecting GSWDs was 94.7% (95% CI 90.1-97.5%) and specificity 99.7% (95% CI 99.3-99.9%).

Conclusions:: An 8-channel EEG can reliably detect GSWDs. In resource-limited settings, 8-channel EEGs may be used by non-specialists to investigate and confirm generalised epilepsy.
ASSESSMENT OF COGNITIVE IMPAIRMENTS IN COMBINATION WITH ANXIETY-DEPRESSIVE DISTURBANCES IN OLD PATIENTS WITH EPILEPSY.

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Background and Aims:: Many recent epidemiological studies have found the prevalence of depression and anxiety to be higher in people with epilepsy. Although cognitive deficits are common in epilepsy, anxiety-depressive disorders and their interaction to cognitive function in older adults with epilepsy is not studied in detail. Our study is aimed to evaluate cognitive disturbances and anxiety-depressive disorders and their relationship in older epileptic patients.

Methods:: We examined 44 older adults with epilepsy (men - 26 (55%) and women - 18 (45%) aged from 56 to 68 years) at the Tashkent Medical Academy in neurology department. The hospital anxiety and depression scale (HADS) was used for determining depression and anxiety disorders. The cognitive impairments were assessed with Mini Mental State Examination (MMSE) scale.

Results:: According to HADS scale, depression was observed in 18 patients (41%), and anxiety - in 26 patients (59%). All patients had severe anxiety. In 38 patients (86%), both depression and anxiety were clinically pronounced (21.67 ± 1.36), in 6 patients (14%) subclinical forms of depression and anxiety were observed (9.56 ± 1.02). According to the MMSE scale, mild dementia (26.17 ± 0.94) was observed in 32 patients (73%), moderate dementia (18.25 ± 1.68) in 12 patients (27%). The level of dementia does not always correspond to the age of patients with epilepsy, but the degree of anxiety and depression, correlates with the severity and duration of the disease.

Conclusions:: The current study identified depression and anxiety as a novel risk factor for cognitive impairments among older adults with epilepsy. Anxiety and depression may be an important treatment target. Therefore, diagnosing and treating anxiety-depressive disorders is of a great importance in old patients with epilepsy, as well as it declines cognitive impairments.
Background and Aims:: The voice changes following VNS implantation may be due to direct injury to the vagus nerve at the time of implantation, these patients present with a true vocal cord paresis, or may result from coactivation of the efferent fibers of the recurrent laryngeal nerve by the VNS. The object of the study was to objectively document the incidence of these two forms of voice disorder following VNS insertion.

Methods:: This prospective study describes 66 consecutive patients between the ages of 3 and 12 years who underwent VNS implantation. At baseline, prior to VNS insertion a Paediatric Voice Handicap Index (PVHI) was performed to assess voice related quality of life, and this was repeated at 3 months following VNS insertion.

Results:: Sixty six patients underwent VNS implantation. Mean age at time of insertion was 90 months. In total 63% of patients reported voice changes, all of which was entirely attributable to the active duty cycle of the VNS device. There were significant changes in the PVHI scores at 3 months follow up. The median change in the PVHI-total score was 2.67 points, and the median change in the PVHI-physical score was 2.12, both of which reached statistical significance (p<0.05). Less significant changes were found in the PVHI-emotional subgroup and functional component of the PVHI scores.

Conclusions:: VNS insertion is associated with a very low risk of true vocal cord paresis, it does however result in significant stimulation dependent alterations in voice related quality of life scores.
EVALUATION OF SUICIDAL IDEATION IN ADULT PEOPLE WITH EPILEPSY AND CAREGIVERS IN A TERTIARY CENTER

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Background and Aims:: Epilepsy is a risk factor for suicidal ideation (SI). SI still poorly investigated in caregivers of people with epilepsy (PWE). We aimed to analyze the prevalence and predictors of SI in adults PWE and caregivers.

Methods:: We analyzed 548 consecutive PWE (60% women; median age 41 [18-83]) and 191 caregivers (72% women; median age 47 [18-82]) followed at Outpatients' epilepsy clinics from a tertiary center. We used “item nine” (item scores ≥1) of the BDI-II to determine the SI presence. The presence of symptoms of anxiety (with BAI) and depression (with BDI-II) was defined with scores ≥14 (for both PWE and caregivers). The presence of anti-seizure drugs (ASDs) adverse effects was defined with the “Liverpool Adverse Events Profile” score ≥46. Epidemiological factors and anxiety were investigated as predictors of SI in caregivers and PWE (along with seizure frequency, epilepsy-type, and ASDs’ adverse events).

Results:: Depression was present in 41% of the PWE and 32% of the caregivers (p=0.04). Anxiety was observed in 37% of PWE and 33% of caregivers (p=0.32). The SI frequency was higher in PWE (19%) compared to the caregivers (11%; p=0.02). Logistic regression analyses were performed for both groups separately. For the PWE (model accounted for 17%-27%), the most significant predictors were anxiety (OR 4.4, p<0.001), presence of ASDs’ adverse effects (OR 2, p=0.021), recurrent seizures (OR 3, p<0.004), and younger age (OR 0.98, p<0.037). For the caregivers (model accounted for 18-37%), only anxiety (OR 43, p<0.001) predicted SI.

Conclusions:: Identifying SI predictors is equally necessary for PWE and caregivers.
Observational Study on Effect of Pulse Intravenous Methylprednisolone in Drug Refractory Epilepsy

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Background and Aims:: Treatment options for management of Drug Refractory Epilepsy are limited and associated with poor results. One of the hypotheses being forwarded for genesis of drug refractoriness in epilepsy is inflammation. In this regard, corticosteroids, well known for their anti-inflammatory and anti-immune properties, have been used with variable results in different epilepsy syndromes. Steroids have also been seen to have a blood brain barrier repair thus helping in better penetration of Anti Epileptic Drugs. Thus, we aim to study the effect of pulse intravenous methylprednisolone in drug refractory epilepsy.

Methods:: All patients >12 years of age diagnosed with drug refractory epilepsy not willing or suitable for surgical treatment excluding the ones with known epileptiform encephalopathies were observed for a period of 6 weeks after their Antiepileptic drugs were optimized to determine seizure frequency. Thereafter, they were given monthly pulse dose of daily methylprednisolone for 5 days and their seizure frequency was noted.

Results:: A total of 22 patients were recruited. Three most consistent risk factors noticed in our study were abnormal MRI, abnormal EEG and history of perinatal distress. There was no significant improvement in any type of seizures after introduction of IV steroids. About 50% of the patients had side effects with one of them had a major side effect of avascular necrosis of left side head of femur.

Conclusions:: Present study did not show any significant beneficial effect of IV methylprednisolone in adult patients with Drug Refractory epilepsy.
SOMATIC COMORBIDITY OF PEOPLE WITH SINGLE SEIZURE IN MOSCOW

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Background and Aims:: The comorbidity of epilepsy is well-known, however the number of studies concerning with comorbidity of people with single seizure (PWSS) are limited. We looked at a somatic comorbidity in PWSS 18 years and older versus controls from Moscow population (MP).

Methods:: It was a case-control study of 70 PWSS (41.69±15.37 years, 32 females) and 211 age- and gender-matched controls (41.85±15.44 years, 95 females). Data source was from the “Unified medical information analytical system” of Moscow. Comorbidities were divided into 14 groups: sleep disorders; severe headache; cerebrovascular disorders; heart diseases; joint diseases; allergies; hypertension; diabetes mellitus; overweight; pulmonary disorders; cancer; ulcer and liver diseases; renal disorders; thyroid conditions. Pearson Chi-square test was used.

Results:: The most prevalent comorbidities in both groups were: arterial hypertension (328.6 per 1000 in PWSS and 241.7 per 1000 in MP) and joint diseases (171.4 per 1000 in PWSS and 170.6 per 1000 in MP). The significant differences between PWSS and MP were found only for ulcer and liver diseases (143 per 1000 in PWSS versus 66 per 1000, p=0.047) and pulmonary disorders (225.6 per 1000 in PWSS and 37.9 per 1000, p=0.000).

Conclusions:: The degree of somatic comorbidity seems to be higher in PWSS versus controls. Further studies are needed for the assessment of comorbidity in PWSS.
Background and Aims:: The study of the clinical and electroencephalographic characteristics of idiopathic generalized epilepsies (IGE) is relevant for accurate diagnosis and subsequent treatment. 

Methods:: Retrospective analysis of 90 continued electroencephalograms (EEG) recorded during wakefulness with the inclusion of functional tests and during sleep in 50 patients with IGE. The Revman 5.3 software with the calculation of the relative risk (RR) was used to compare the groups. Differences were considered significant at p>0.05.

Results:: The study included 12 patients with childhood absence epilepsy (CAE) (24% of all patients), juvenile absence epilepsy (JAE) – 12(24%), juvenile myoclonic epilepsy (JME) – 13(26%), epilepsy with isolated generalized seizures (EGS) – 13(26%). The index of generalized epileptiform activity (GEA) is higher during wakefulness than during sleep in CAE, JAE, JME. There are no differences in the activity index for CAE, JAE, JME when compared during wakefulness and sleep, but the GEA index is higher in sleep in CAE, JAE, JME compared to EGS: RR=0.12 [0.02, 0.81], p=0.03; RR=0.24 [0.06, 0.90], p=0.03; RR=0.33 [0.12, 0.96], p=0.04, respectively. In patients without seizures, GEA continues: CAE–33%, JAE–38%, JME–36%, EGS–33%.

Conclusions:: With EGS, epileptiform activity is more common in sleep than during wakefulness, in CAE, JAE and JME, GEA occurs more often during wakefulness and functional tests than in sleep. More than 30% of patients with IGE with clinical remission, regardless of the form, have GEA on the EEG. The study was funded by Russian Foundation for Basic Research (RFBR) according to the research project №17-29-09096.
FEATURES OF PHARMACORESISTANT EPILEPSY IN NEUROSURGICAL PATIENTS

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Background and Aims:: Epilepsy is one of the most common and stigmatizing diseases. The aim of the present study is to investigate the features of pharmacoresistant epilepsy in neurosurgical patients.

Methods:: We conducted a cohort study of clinical and demographic parameters among neurosurgical patients with verified diagnosis of pharmacoresistant epilepsy.

Results:: The final sample included 91 case histories of patients who underwent neurosurgical intervention for pharmacoresistant epilepsy. Particular attention was paid to the duration of the disease. According to the duration of the disease before admission to the hospital for neurosurgical treatment, patients were distributed as follows: 3-5 years - 7% (6 people), 6-10 years - 16% (15 people), 11-20 years - 36% (33 people); for more than 20 years, - 41% (37 patients) suffered from drug-resistant epilepsy. The analysis of the data obtained showed that this category of patients is characterized by a long history of the disease and a late request for neurosurgical help. When assessing the severity of seizures, it was found that with an increase in the duration of epilepsy, seizures become more severe and their frequency increases. There was also a tendency towards bilateral spread of pathological epileptiform activity on the EEG with a duration of illness of 10 years or more.

Conclusions:: The duration of epilepsy before admission to a neurosurgical hospital is a manageable indicator - this fact requires finding a solution to the problem of faster referral of patients with drug-resistant epilepsy for pre-surgical examination.
SODIUM VALPROATE INDUCED HYPERAMMONEMIC ENCEPHALOPATHY PRESENTING WITH PERSONALITY CHANGES AND DRESSING APRAXIA

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Background and Aims: Sodium valproate is a widely used antiepileptic agent in practice and is rarely associated with hyperammonemia

Methods: Case report A 49 year old businessman with a history of adult onset epilepsy for last two years presented with behavioral changes since last 2 months. His family members complained of recent onset forgetfulness, changes in his personality and dressing apraxia. He had been started on Sodium valproate 200 mg twice daily and Carbamazapine 200 mg twice daily 2 years back when he developed generalized tonic clinic seizures. Recently Sodium valproate dose had been increased to 400 mg twice daily as he had a break through seizure. On examination he had loss of executive function, memory impairment and dressing apraxia. His Mini mental status examination was 15/30. At this point his serum ammonia level was 84 μmol/L (26.6-47 μmol/L). His MRI brain was normal. He was started on Levetiracetam after stopping valproate and his behavior shifted back to normal. Repeated values after 1 month and 3 months of stopping sodium valproate were 55 μmol/L and 35 μmol/L. Rest of his liver function tests and abdominal ultrasound scan were normal.

Results: Discussion Valproate induced hyperammonemia is very rare and considered as an idiosyncratic reaction. Valproate can cause hyperammonemia without altering the other liver function tests.

Conclusions: Being aware of this rare side effect of valproate and monitoring serum ammonia level if suspected will be helpful in the clinical practice
THE INCIDENCE OF ADVERSE DRUG REACTIONS IN MONOTHERAPY OF EPILEPSY WITH VALPROIC ACID: GENDER DIFFERENCES

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Background and Aims:: Adverse drug reactions (ADR) in patients treated with antiepileptic drugs (AEDs) require the study of gender differences. We present the retrospective analysis of ADR registered in medical records of patients who received monotherapy with valproic acid (VA) in 2015-2020.

Methods:: 184 patients (76 males, 108 females) were included into research (111 aged 18-, 73 aged 18+). Statistical processing: Excel (MS Office 2017), Statistica 10.0 software packages. The Revman 5.3 software with the calculation of the relative risk (RR) was used to compare the groups. The differences were considered significant at p<0.05.

Results:: ADR were in 111/184 (60.3%) patients treated by VA, 42/111 (37.8%) male and 69/111 (62.2%) female. 186 ADR were registered. The average age (AA) in patients with ADR is lower than in patients without ADR. Statistically significant differences (SSD) were found in general group (GG)(p=0.0006), in 18-(p=0.0001), in 18+(p=0.003). The same is observed in men: GG(p=0.01), 18(p=0.01). AA in women with ADR is also lower than in women without ADR in GG(p=0.01), 18-(p=0.003), 18+(p=0.002). In patients with ADR, the average daily doses of VA are higher than in patients without ADR. SSD were found in GG(p=0.04), 18+(p=0.03). Higher doses of valproate were in men with ADR in GG (p=0.008), in women with ADR in 18+(p=0.03) compared with patients of the same gender without ADR.

Conclusions:: A retrospective analysis showed the presence of gender differences of ADR in patients treated by VA. The study was funded by Russian Foundation for Basic Research (RFBR) according to the research project №17-29-09096.
SEXUAL DYSFUNCTION IN MEN WITH EPILEPSY

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Background and Aims:: Sexuality and epilepsy have been intimately linked since ancient time. Disturbances of reproductive and sexual health are common in men with epilepsy (MWE). This study aimed to evaluate the role of antiepileptic drugs in the genesis of erectile dysfunction and to determine the therapeutic implications of this complication.

Methods:: This was a cross-sectional study including MWE aged from 18 to 59 years old. Erectile function was assessed using the International Index of Erectile Function Questionnaire (IIEF-5) and the EQS questionnaire (erection quality scale). We have also defined therapeutic implications of this complication.

Results:: 157 MWE were included in our study. Among 109 patients on valproate monotherapy, 10.9% developed erectile dysfunction. Carbamazepine (CBZ) was associated with erectile dysfunction in 5.40% of cases. Phenobarbital had no effect on male sexuality. Among 76 men on polytherapy, this complication was noted in 6.57% of cases. 85.7% of patients having erectile dysfunction requested to switch the treatment. Poor adherence to therapy was described in 67.85% of these patients.

Conclusions:: Reproductive dysfunction is common among MWE. Both epilepsy and AEDs have been causally implicated. Our study highlights the negative effects of anti-epileptic drugs on erectile function. Thus, an evaluation of erectile function in men with epilepsy is necessary.
SAFETY AND TOLERABILITY OF ADJUNCTIVE ESLICARB AZEPINE ACETATE IN ADOLESCENTS WITH FOCAL-ONSET SEIZURES: DATA FROM THREE DOUBLE-BLIND, PLACEBO-CONTROLLED RANDOMIZED CLINICAL STUDIES

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Background and Aims:: Adolescence is a critical developmental period in which major metabolic changes occur.¹ We aimed at evaluating safety and tolerability of adjunctive eslicarbazepine acetate (ESL) in adolescents (ages 12-18) with refractory focal-onset seizures.

Methods:: Safety and tolerability data from Part I of studies BIA-2093-208 (phase II), -304 and -305 (Phase III)²-⁴ were pooled and analysed through the evaluation of treatment-emergent adverse events (TEAEs). These were randomized, double-blind, placebo-controlled studies of adjunctive ESL (1–2 antiseizure concomitant medications) in patients with refractory focal-onset seizures.

Results:: The safety population of the studies comprised 1077 patients, of which 186 (17.3%) were adolescents (n=73 placebo; n=113 ESL-arms). From the 186 patients, n=69, n=20 and n=97 were from BIA-2093-208, 304 and 305, respectively. The incidence of any TEAE was 10.7% (n=45) and 10.9% (n=72) of patients in placebo and ESL-arms, respectively; while related TEAEs were reported by 4.5% (n=19; placebo) and 5.2% (n=34; ESL-arms) of the patients. Most frequent related TEAEs were: somnolence (5.5% placebo; 8.0% ESL-arms), vomiting (0.0% placebo; 5.3% ESL-arms), diplopia (2.7% placebo; 3.5% ESL-arms), fatigue (4.1% placebo; 2.7% ESL-arms) and nausea (1.4% placebo; 4.4% ESL-arms). One patient (0.2%) in placebo arm experienced a serious related TEAE (convulsion). Three patients (0.5%) suffered related TEAEs leading to discontinuation in ESL-arms (1 patient: dermatitis allergic; 1 patient: asthenia, vomiting and nausea; 1 patient with oedema). No TEAEs led to death.

Conclusions:: Treatment with adjunctive ESL in adolescents with refractory focal-onset seizures was generally well-tolerated. The safety profile was consistent to the observed in adults, with no new findings.
EPILEPSY IN CHAD: THE EXPERIENCE OF THE NATIONAL REFERENCE TEACHING HOSPITAL

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Background and Aims:: Epilepsy remains a major public health problem in developing countries of development. However, it has received very little attention in Chad. To my knowledge, this is the first sighting reported in this country. We report the observations in order to describe the socio-demographic, clinical and therapeutic characteristics of epilepsies.

Methods:: We report a prospective and descriptive study lasting one year ranging from November 1st, 2019 to October 31st, 2020, carried out at the Neurology Unit of National Reference University Hospital Center. All patients seen for epileptiform manifestation during the study period were included. Socio-demographic, clinical, paraclinical and therapies were identified and analyzed using SPSS 2.0 software. P value <0.05 was considered significant.

Results:: Out of 603 observations, 532 patients (208 children and 258 women) responded to the diagnostic criteria. The mean age was 30 ± 16.9 years. Among adults, 24% were out of school, 19% had left primary school. Twenty-three school-age children were out of school. Fifty six patients had reported a history of head trauma followed by family history (31 patients) and meningitis (26 cases). Generalized seizures (62.2%), seizures of unknown onset (20.7%) and focal seizures (17.1%) were reported. The electroencephalogram was performed in 319 patients, computed tomography in 120 patients and MRI in 7.3% of cases. The cryptogenic causes were the most reported (46.6%) followed by causes symptomatic (40.6%). Phenobarbital (37.8%), carbamazepine (32%) and sodium valproate (22.6%) were used.

Conclusions:: The management of epilepsy remains a major problem, due to the awareness of the population, diagnosis, treatment and follow-up of patients.
EPIDEMIOLOGICAL, CLINICAL AND COMPARATIVE STUDY OF NEUROCOGNITIVE AND SLEEP DISORDERS IN PATIENTS WITH ONCHOCERCIASIS-ASSOCIATED EPILEPSY IN THE MONATÉLÉ HEALTH DISTRICT, CENTER REGION OF CAMEROON.

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Background and Aims:: Over the past decade, there has been mounting evidence from Onchocerciasis-endemic regions in Africa that onchocerciasis causes epilepsy. The term Onchocerciasis-associated epilepsy (OAE) has been used to describe this condition. Few studies have been done in our context to quantify the burden of onchocerciasis-associated epilepsy.

Methods:: This was a cross-sectional study conducted in an onchocerciasis-endemic zone in Cameroon. Door-to-door household visits were carried out to screen for persons with OAE. Clinical sleep and neurocognitive scales were used to screen for sleep disorders and neurocognitive disorders respectively.

Results:: In all, 1448 individuals from 202 households were screened. Fifty persons met the criteria for OAE and were included in the study. The crude prevalence of OAE was 4.7%. The most common seizure type was generalised tonic-clonic seizures. Sleep onset insomnia was the main sleep disorder. The main factors associated with sleep disorders were older age, female sex and having sand extraction as occupation. The most commonly affected cognitive functions were memory, verbal fluency, attention and executive functions. Factors associated with poorer neurocognitive outcomes were longer duration of epilepsy, frequent seizures, low educational level, generalised tonic-clonic seizures and early age of onset of epilepsy.

Conclusions:: The prevalence of OAE constitutes an additional argument for strengthening onchocerciasis elimination efforts in Cameroon and Africa.
TARGETING P-Glycoprotein Efflux Transporter Via the Selective COX2 Inhibitor Celecoxib Improves Levetiracetam Clinical Response in Epilepsy

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Background and Aims:: One of the major drug efflux transporters of concern in drug resistant epilepsy (DRE) is P-glycoprotein (P-gp). P-gp's reported overexpression in epileptic foci resected from patients intensifies its intimate link to DRE. The principal aim of the study was to assess the importance of P-gp as a potential therapeutic target in epilepsy. Can expression modulation of P-gp by celecoxib boost the antiepileptic effect of the P-gp substrate; levetiracetam?

Methods:: Forty epilepsy patients were included in a 3 month-prospective study. Patients were on levetiracetam 3000 mg/day. They were randomly allocated into two groups; levetiracetam only group including levetiracetam treated patients and levetiracetam + celecoxib group including patients on levetiracetam with add-on oral celecoxib 200 mg/day to be given daily in the last week of every month till the end of the study. During the 3 months of the study, four outpatient clinic visits were performed for each patient: A 1st baseline visit and 3 monthly follow-up visits. Clinical response was estimated by recording each patient's seizure frequency/month. For assessment of P-gp mRNA expression level, venous blood sampling was withdrawn from every patient twice (on the first and last visits).

Results:: At the end of the last month, levetiracetam only group showed a non-significant decrease in P-gp expression and seizure frequency compared to the 1st month. Whereas, in levetiracetam + celecoxib group, P-gp expression was significantly reduced and associated with a significant seizure control.

Conclusions:: Celecoxib by downregulating P-gp overexpression can improve levetiracetam brain availability and hence its clinical effect.
CHANGES IN THE CELLULAR COMPOSITION OF THE HIPPOCAMPUS IN DRUG-RESISTANT EPILEPSY

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Background and Aims: Hippocampal sclerosis (HS) is a common morphological substrate in drug-resistant temporal lobe epilepsy. According to the classification of HS, developed by ILAE in 2013, this pathology is characterized by disorders of the cellular structure of the hippocampus, neuronal death and gliosis. The role of the hippocampus in epileptogenesis and the pathogenesis of HS are still unclear.

Purpose: To assess changes in the cellular composition in the hippocampus in patients operated on for drug-resistant epilepsy.

Methods: 17 patients with drug-resistant epilepsy at the age of 22 to 54 years. 6 women and 11 men, the average age of the patients was 34.4 years, the average duration of the disease was 18.7 years. The comparison group included patients who died from pathology that did not affect the central nervous system: 2 women and 5 men, the average age of the patients was 70.1 years.

Results: In 85.7% of patients focal cortical dysplasia of various types was found in the temporal lobe. The number of neurons in the dentate gyrus in patients with drug-resistant epilepsy and in the comparison group is significantly different according to Mann–Whitney U test (p <0.05). A significant correlation r = 0.54 was obtained in the conjugation of glial density in the CA1 and CA4 nuclei in all patients.

Conclusions: The revealed structural changes in the hippocampus in patients with drug-resistant epilepsy were characterized by elective neuronal death with a predominant lesion of the dentate gyrus.
THE ROLE OF A SHARED DECISION-MAKING PROCESS IN PAEDIATRIC EPILEPSY SURGERY

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Background and Aims:: Around thirty percent of children with epilepsy will become drug resistant and therefore potential surgical candidates. Little is known about parental decision making for/or against epilepsy surgery. Shared Decision Making (SDM) involves the collaboration of health care professionals and patients through a structured process that considers best evidence and patient values. Our aim is to determine if a shared decision-making process assists the family in knowledge and improves satisfaction when making an epilepsy surgical decision.

Methods:: A quality improvement project was initiated at our hospital where epilepsy surgical candidates were identified by the paediatric epileptologist and referred to the SDM coach. These visits provided patients/families with evidence-based education materials tailored to their specific decisional needs to assist with surgical choices. The decision process was assessed utilizing a Decisional Conflict Scale, the Ottawa Family Decision Guide, Preparation for Decision Making Scale, and the post Decision Coach Questionnaire.

Results:: Fifty families were offered SDM Coaching consults, forty-five families completed initial visits. The primary issue pre-test was mainly focused on needing more knowledge about the risks, benefits and options. All families were clear about their personal values and felt supported to make a choice but were unsure about risks/benefits for their child. Post consult scales on satisfaction/knowledge levels indicated a high level of preparation post consult.

Conclusions:: Although epilepsy surgery is a curative procedure in drug resistant epilepsy, families often experience anxiety, uncertainty and decisional conflict. SDM assists families in their need for more knowledge regarding risks, benefits for treatment prior to making a surgical choice.
SCHIZOPHRENIA FOLLOWING SUPER-REFRACTORY STATUS EPILEPTICUS (CASE SERIES)

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Background and Aims:: We are reporting new-onset schizophrenia following super-refractory status epilepticus in five cases to increase awareness about this rare complication of super-refractory status epilepticus.

Methods:: Case Series

Results:: All cases were seen in King Faisal Specialist Hospital and Research Center in Riyadh, Saudi Arabia, a tertiary center. Four males and one female. Their ages range between 20 and 46. They shared some clinical features, including that; they don’t have a history of epilepsy or its risk factors, all had super-refractory status epilepticus, lack a prior history of any mental illness or schizophrenia risk factor, and all of them developed schizophrenia at least 2-4 weeks after they recovered from status epilepticus. Four patients; their status epilepticus was secondary to autoimmune etiology, and one was secondary to viral encephalitis. Four patients had MRI T2/FLAIR hyperintensity in temporal lobe and other brain regions. Only one patient had a normal MRI brain. Three patients had abnormal CSF. Four patients were immunocompetent, and one patient only was immunocompromised (post-liver transplant). All patient is following with psychiatrist, and the majority of them are on antipsychotics. One patient has severe schizophrenia and refractory to medications.

Conclusions:: Schizophrenia following new-onset super-refractory status epilepticus is a rare complication of super-refractory status epilepticus.
SYSTEMATIC REVIEW OF THE ONGOING CLINICAL TRIALS EVALUATING THE UTILITY OF BRIVARACETAM ACROSS VARIED PATIENT POPULATION

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Background and Aims:: Brivaracetam is currently approved for the treatment of partial-onset seizures in patients 4 years of age and older. The aim was to systematically evaluate study designs and outcomes being analysed in the ongoing trials evaluating brivaracetam across varied patient profiles.

Methods:: Two independent researchers reviewed contemporary protocols of trials currently recruiting patients for ongoing trials, through WHO- ICTRP (www.who.int/ictrp/search/en), www.clinicaltrials.gov trials registry databases. The latest evaluation was on April 10, 2021.

Results:: There are four trials registered in Japan registry of clinical trials and five in clinicaltrials.gov. All are multicentric studies across North America, Europe and Asia. The mean number of patients being enrolled is 177 (SD ± 146, maximum 444, minimum 10, range 434, 95% CI 42 to 312). Cumulatively, 1237 patients are targeted across seven unique trials. Two trials are evaluating brivaracetam in the pediatric population (cumulative n=142) with seizures. The extreme ages range from newborn to 80 years. The five trials in adults are enrolling patients with partial seizures with or without secondary generalization, epilepsy, and safety and tolerability of intravenous brivaracetam as a replacement for oral brivaracetam. There are six interventional phase 3 trials and one observational study. The primary endpoints include adverse events, change in seizure frequency, plasma concentration of brivaracetam

Conclusions:: Brivaracetam is distinctively being evaluated for pediatric population with age less than 4 years. The emerging outcomes, for brivaracetam, across the varied patient population, being evaluated, across the World appears to add to the current strength and level of published evidence especially in the pediatric age group
COMPARING PREVALENCE OF STATIN PRESCRIPTION BETWEEN ENZYME INDUCING ANTIΕPILEPTIC DRUGS VERSUS NON-ENZYME INDUCING ANTIΕPILEPTIC DRUGS IN ADULT PEOPLE WITH EPILEPSY: A PRELIMINARY STUDY

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Background and Aims:: There are many cross-sectional studies that people with epilepsy (PWE) taking enzyme-inducing antiepileptic drugs (EIAEDs) may have higher cholesterol levels. There is also a report that PWE taking EIAEDs have more chance to have statin prescription compared to PWE taking NEIAEDs. The aim of this study is to compare statin prescription prevalence between EIAEDs versus NEIAEDs among PWE in South Korea.

Methods:: We investigated the prevalence of statin prescription among adult PWE by using the claims data of the Health Insurance Review and Assessment Service-National Patients Sample. To minimize the bias of other drug’s effects, PWE who were treated with only monotherapy of carbamazepine (CBZ), phenytoin (PHT), levetiracetam (LEV), and lamotrigine (LTG) were included. PWEs having comorbidity were excluded because these patients have higher chance of taking statins without high cholesterol levels.

Results:: The enrolled number of adult PWE who were treated by AED monotherapy was 2760 in 2014. Among these patients 1056, 288, 877, and 539 patients were treated with CBZ, PHT, LEV, and LTG respectively. The prevalence rates of their statin treatment were 5.1, 3.5, 3.8 and 2.0 % in CBZ, PHT, LEV, and LTG respectively (p=0.026). Among EIAEDs (CBZ+PHT) users, 4.8 % received statin therapy, compared with 3.1 % of those who take NEIAEDs (LEV+LTG) (p=0.025).

Conclusions:: This study showed that PWE taking EIAEDs by monotherapy may have a higher tendency to take statins than those taking NEIAEDs in South Korea, 2014. Further risk-controlled and longitudinal studies will be needed.
OPTIMIZATION OF TREATMENT OF CATAMENIAL EPILEPSY IN WOMEN

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Background and Aims:: Optimization of the treatment algorithm for catamenial epilepsy in women of fertile age.

Methods:: All examined patients underwent included the study of the neurophysiological studies, laboratory studies of the level of female sex hormones during one cycle in the follicular and luteal phases. To optimize therapy, taking into account the minimal effect of topiramate on the development of oncological diseases of the female reproductive system, we gradually replaced the anticonvulsant drug valproic acid with topiramate at the rate of 3-5 mg/kg of body weight per day. At the same time, the average daily dose did not exceed 200 mg/day.

Results:: After 6 months of regular administration of topiramates at a dosage of 200 mg / day, the first group of patients showed a decrease in the frequency of attacks from 8-10 to 5 attacks per month. In addition, patients noted a decrease in the duration of seizures up to 1 minute, with initial values up to 3-5 minutes. In the second group, we also noted a decrease in the frequency of seizures up to 3-4 times a month. Studies have shown that the use of topiramates led to a decrease in estrogen levels and an increase in progesterone levels, which contributed to a decrease in the frequency of epileptic seizures.

Conclusions:: The results of our studies of changes in hormonal status revealed fluctuations in indicators in the follicular and luteal phases, which were positive against the background of taking topiramate. In the second group, our studies showed no positive effect of valproic acid on the change in the progesterone/estradiol ratio.
THE FREQUENCY OF EPILEPTIC SEIZURES IN PERSONS OF UZBEK NATIONALITY AND THE USE OF ANXIOLYTICS

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Background and Aims:: Epilepsy is a chronic disorder, which is recurrent, unprovoked seizures. A person is diagnosed with epilepsy if they have two unprovoked seizures (or one unprovoked seizure with the likelihood of more) that were not caused by some known and reversible medical condition. The seizures in epilepsy may be related to a brain injury or a family tendency, but often the cause is unknown. Many people with epilepsy have more than one type of seizure and may have other symptoms of neurological problems as well.

Methods:: There were studied Uzbek patients which were hospitalized for the period 2018-2020. For researching were selected patients with prescription of the disease 10 and more years. Special attention was given to the age when the first signs appeared.

Results:: Gender analysis determined that women`s quantity dominated (55.07%, mean age 24±5.3 years), men's 44.93% (61.2%, mean age 26±3.2 and 38.7% with mean age 46±4.8 years). Average duration of seizures 8.5-12.1 minutes. The frequency of recurrent seizures in women from 25.43% to 30% per year. For men this indicator was equal to 17.2-20.3%. In 2.03% of men and 2.63% of women, convulsions recurred 2 times a month. In 2.15% of men and 3.5% of women were repeated 2 times a day. In each of the above cases, the anxiolytic (tranquilizer) “Sybasoni 0,5%” was used.

Conclusions:: The analysis of the register of epilepsy in Uzbek people demonstrated that epilepsy seizures was the most common disease in women (55.07%), in all patients used anxiolytic.
COMPARATIVE ANALYSIS OF EFFICIENCY OF SOME ANTIEPILEPTIC DRUGS MONOTHERAPY WITH THE ASSESSMENT OF THE DYNAMICS OF QUALITY OF LIFE IN PATIENTS WITH EPILEPSY

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Background and Aims: It is known that the frequency of seizures, working abilities and associated mental disorders are revealed to be risk factors for the QOL (quality of life). To evaluate the QOL of epilepsy patients with estimating its dynamics on the background of monotherapy with some AEDs (antiepileptic drugs) in the Republic of Uzbekistan.

Methods: Study included 52 patients aged 18-44 (23 men, 29 women). All patients completed a questionnaire QOLIE-31 before and after 4 months of beginning the therapy or its optimization.

Results: All patients were receiving monotherapy with following AEDs: Carbamazepine- 37%, Valproate-37%, Topiramate - 15%, Lamotrigine - 11%. Comparing total score of QOL in groups showed that the largest number of patients rated their QOL as the highest observed in groups treated with Lamotrigine (80%), Topiram (75%), Depakine (70%). At patients receiving Carbamazepine it was adequate to the good QOL (40%). The most significant anti seizure efficiency among all groups of drugs demonstrated Topiramate, the frequency of clinically significant side effects and negative impact on QOL were not observed, which does not distinguish it from Valproate, moreover, degree of changes in subscales “Emotional well-being”, “Cognitive functioning” in the course of treatment was significantly higher than in patients receiving Carbamazepine, Lamotrigine and Valproate.

Conclusions: A comparative evaluation of QOL before treatment, showed it was similar in all groups. The greatest anti seizure effect was detected in Valproates. The greatest influence on individual subscale , total score of QOL - at patients received monotherapy with Valproate or Lamotrigine, lower QOL were in other groups.
SEIZURE CONSEQUENCES AND PREDICTORS OF RECURRENCE POST-STROKE SEIZURE

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Background and Aims:: Seizure is considered one of the worst Post Stroke Complications. There is not any confidential predictors of Post Stroke Seizure (PSS) recurrence although many scientists have estimated outcomes and risk factors of PSS. In order to prognosis degree of recurrence, we compare baseline clinical characteristics and Post Stroke treatment regimens between recurrent and non-recurrent PSS patients.

Methods:: The retrospective cohort study included 75 patients with PSS that admitted to Clinic of Tashkent Medical Academy between June 2017 December 2019. Analyzed baseline clinical characteristics and recurrence rate. Cumulative recurrence rates at 80, 160, and 320 days post-stroke were evaluated by Kaplan—Meier analysis. Sovereign predictors of recurrent PSS were identified by Cox proportional-hazards analysis.

Results:: Overall 75 patients (42 men; 38 women medium age, 70.1±11.2 years) were analyzed. PSS recurred in 22 patients (30%) during the follow-up. Factors significantly associated with PSS recurrence by log-rank analysis included previous PSS, valproic acid (VPA) monotherapy, polytherapy with antiepileptic drugs (AEDs), frontal-parietal cortical lesion, and higher modified Rankin Scale score at discharge (all p<0.05). Independent predictors of recurrent PSS were age<72 years (HR 3.11, 95% CI 1.41–6.02), VPA monotherapy (HR 5.78, 95% CI 2.45–13.89), and convulsions on admission (HR 4.21, 95% CI 2.06–14.21).

Conclusions:: Approximately one-third of PSS patients experienced seizure recurrence within one year. The predictors of recurrent PSS were younger age, presence of convulsions and VPA monotherapy. Our findings should be interpreted cautiously in countries where monotherapy with second-generation AEDs has been approved because this study was conducted while second-generation AEDs had not been officially approved for monotherapy in Uzbekistan.
PERAMpanel Effectiveness and Tolerability in Patients with Epilepsy at Long-Term Follow-Up

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Background and Aims:: Assess the effectiveness and tolerability of perampanel (PER) in association with one or two concomitant antiseizure medications (ASMs) in patients with epilepsy throughout a follow-up of 24 months or longer in a real-world setting.

Methods:: This retrospective, observational, multi-centre study collected data from both underage and adult patients who started PER in association with one or two ASMs and were followed for at least 24 months. Patients who interrupted PER in the first 3-month were excluded. Response to treatment was analysed at 24-, 36- and 48-month visits by considering the last visit. Subgroup analyses were performed according to age, gender, epilepsy type and number of concomitant ASMs to evaluate the factors influencing seizure freedom (SF) achievement at 24-month.

Results:: Ninety patients (95.74%), of the initial 94, were still continuing PER concomitantly with 1 or 2 ASMs at 24-month follow-up (mean age 36.89 years; 51.1% female). SF was achieved by 33 (35.1%) patients. Patients who started PER with only one ASM had a higher SF rate compared to those who started PER with two concomitant ASMs. Effectiveness was maintained also in the subgroups of patients with a 36- or 48-month follow-up. A lower number of previously failed ASMs was associated with a higher SF rate.

Conclusions:: PER demonstrated good effectiveness in association with one or two ASMs in both paediatric and adult patients. The possibility to present SF was higher when PER was added early. The maintenance of effectiveness was observed also in the subgroups of patients with a follow-up of 36 and 48 months.
A CASE OF MYOCLONIC STATUS EPILEPTICUS IN A PATIENT WITH BRAIN METASTASES: ROLE OF DYSFUNCTION OF THE THALAMUS-CORTICAL NETWORK AND INHIBITION OF THE SOMATOSENSORY CORTEX

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Background and Aims:: We present the case of a 55-year-old woman with chemo-treated left breast cancer and brain metastasis, who developed a myoclonic status epilepticus in conditions of full well-being. The patient came to our attention due to the onset of short episodes characterized by dysautonomia and motor stereotypies in the upper limbs. During the electroencephalographic recording, the patient presented a narrowing of the state of consciousness, followed by erratic and diffuse myoclonia, initially in the eyelids and with subsequent involvement of the axial, laryngeal-phonatory muscles and of the upper limbs, and finally by the appearance of motor automatisms. In a peculiar way, the tactile stimulation of the upper limbs induced a gradual reduction of the diffuse epileptiform anomalies, up to their complete regression.

Methods:: EEG showed the sudden appearance of spikes and irregular sharp-wave complexes on the bilateral fronto-central regions and at the vertex, with subsequent bihemispheric diffusion. MRI showed the presence of a metastatic lesion in the left nucleobasal site, characterized by inhomogeneous post-contrast enhancement with an abundant amount of perilesional vasogenic edema.

Results:: Levetiracetam therapy was started at a dose of 2000 mg/day, with clinical benefit.

Conclusions:: We discuss the hypothesis that the nucleobasal lesion, in close proximity to the thalamus, may have triggered the myoclonic state through a dysfunction of the thalamo-cortical network, with ictal activation of the primary motor cortex. Furthermore, we assume that the activation of the sensorimotor cortex triggered by tactile stimulation may have helped inhibit the dysfunctional epileptic circuit of the motor cortex, with remission of the electroclinical picture.
THE PROGRESS OF CONVULSION SYNDROME IN PATIENTS WITH HIV INFECTION

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Background and Aims:: The aim of the study was to identify the causes of convulsive syndrome and investigate the characteristics of the progress in HIV-infected patients.

Methods:: The study is based on survey data among 25 HIV-infected patients with convulsive syndrome.

Results:: In terms of gender composition, men prevailed women, on average age was 35±2.5 years old. Among patients, 2 suffered from convulsive syndrome associated with alcohol withdrawal, the other 23 patients suffered from structural-metabolic and symptomatic forms of focal epilepsy. Among 25 patients: 12 (48%) of them knew their HIV-positive status before going to a neurologist, in 7 (28%) patients, the diagnosis was clarified upon admission to a neurosurgical hospital, in 6 (24%) patients HIV infection was diagnosed after the development of neurological complications (epileptic seizures, movement disorders). In 17 (68%) patients, seizures occurred before the diagnosis of HIV infection and in 8 (32%) patients after the infection. During hospitalization in a neurological hospital, patients often required a long diagnostic search to establish diagnosis of toxoplasmosis and HIV-associated leukoencephalopathy. The causes of epileptic seizures in these patients are different, among them, in 8 patients epilepsy developed as a complication of HIV infection in the CNS, HIV-associated leukoencephalopathy observed in 7 patients, 1 patient was diagnosed with toxoplasmosis.

Conclusions:: Seizure syndrome is an often-disabling complication of HIV infection. Early diagnosis of the disease and good patient compliance make it possible to achieve early drug remission of the convulsive syndrome.
SPECIFICATIONS OF EPILEPSY AND CEREBRAL PALSY IN CHILDREN

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Background and Aims:: Determine the features of epilepsy with cerebral palsy in children and study clinical electroencephalography in this patients.

Methods:: We examined 70 children (from 1 to 16 years old) patients with various types of cerebral palsy and epilepsy in children. Research work was done at Tashkent Medical Academy Clinic’s Neurology Department. All patients underwent clinical examination, electroencephalography, computed tomography (CT), video-EEG monitoring and MRI.

Results:: From the all patients, only in 7.3% occurred epilepsy. The most common epilepsy with cerebral palsy was detected in age from 9 months to 3 years - 31.4% (22 children). At the age of 5 to 7 years it turned 22.9% (16), from 7 to 10 years - 20% (14), from 10 to 15 years - 14.2% (10 children) and teenagers from 14 to 17 years - 11.5% (8). With a little epilepsy prevalence was recorded in boys with cerebral palsy - 48.7%. Among all patients with cerebral palsy revealed a high incidence of epilepsy with spastic forms (double hemiplegia, spastic diplegia) to 69.7%. In children with hemiplegia and found 18.8% with other forms of cerebral palsy (atonic-astatic, hyperkinetic, mixed) - 11.5%. There were prevailed myoclonic seizures, tonic axial symmetric tonic spasms, multifocal, secondary generalized seizures in infants and early childhood.

Conclusions:: Diagnostic features of epilepsy in children with cerebral palsy has led to the achievement of rapid detection of seizures in 72.5% of patients, which made it possible to provide the rehabilitative treatment of children with cerebral palsy.
FEATURES OF EPILEPSY IN DIFFERENT GROUPS OF PATIENTS IN UZBEKISTAN

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Background and Aims:: The aim of this study was to investigate the features of different types of seizures in group of patients in Uzbekistan

Methods:: The work is based on the results of examination of 85 patients with epilepsy (45 men and 40 women - 53.0% and 47.0%, respectively). Patients underwent a neuropsychological study, as well as neuroimaging techniques.

Results:: We observed a group of patients older than 50 years with epilepsy that began at a young and middle age. In three cases, a remission of the disease is achieved, in one, seizures are recorded with a frequency of 1 per year - one and a half years. In symptomatic and cryptogenic variants with only secondary generalized seizures, remission was achieved in only 3 cases (15.8%), rare seizures and drug-resistant frequent seizures were recorded in half of the cases and in 36.8% of patients respectively. Focal epilepsy dominate the structure of epilepsy in patients of mature age and elderly, of which symptomatic forms reach 83.9% of epilepsy and are more common than in middle age. Significantly more often in this age group there is a secondary generalization of seizures (>71.6%).

Conclusions:: In patients of mature age and elderly, mainly focal seizures with or without secondary generation are observed, in our study up to 90.0%, we did not receive the predominance of complex partial seizures in the elderly. Secondary generalization in this age of group reaches 71.6%, which is less than in children and young men. Diagnosed ideopathic generalized epilepsy in adulthood and old are rare.
DIFFERENCES BETWEEN MEDIAL AND LATERAL TEMPORAL LOBE EPILEPSY

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Background and Aims:: Aim of the research work was to study the differences between the changes of medial and lateral temporal lobe epilepsy (MTLE and LTLE).

Methods:: For the research work we were examined 48 patients with medial and lateral temporal epilepsy, who were on a stationary examination in the department of neurology of the multidisciplinary TMA clinic. During Video-EEG-monitoring we recorded 114 seizures of various types.

Results:: The most significant lateralizing features in this form of epilepsy were one-sided wrist automatism, a dystonic brushes and an unbalanced turn of the head. The most valuable lateralizing sings of the epileptogenic focus for this form of epilepsy are the dystonic setting of the wrist (85.7%, p = 0.02), the inverting turn of the head (88.9%, p=0.02) and after-seizure aphasia (100%). Also for this group, the prevalence of localization of pathological disturbances in the region of the anterior temporal electrode was found (75.0%, p = 0.02 in comparison with the LTLE group), and in cases of presence of additional zones of localization - their registration in the contralateral temporal lobe (63.6%, p=0.02 in comparison with the LTLE group).

Conclusions:: Taking into account the revealed features of seizures, differential diagnosis between lateral and medial forms of temporal epilepsy can be based on the lateralizing sings.
Background and Aims:: Introduction: Bone fractures in epileptic patients may be associated with trauma either induced directly by a seizure or resulting from a fall or other accident resulting from the seizure. In themselves, seizures can induce fractures of the femoral neck, humeral head, acetabulum, scapula, or vertebral column by violent contractions of skeletal muscles.

Methods:: CASE DESCRIPTION We describe a 48-year-old male with severe back pain from a lumbar fracture occurring in association with a seizure during hospitalization for treatment of renal inefficiency. Bone mineral densities in the lumbar spine and the femoral neck were normal. Bone Scintigraphy and tumour marques levels were normal. Patient underwent an orthopedics treatment with lumbar orthosis and bed rest for 2 months; radiographic control 3 months later demonstrated good respect of lumbar lordosis.

Results:: CASE DESCRIPTION We describe a 48-year-old male with severe back pain from a lumbar fracture occurring in association with a seizure during hospitalization for treatment of renal inefficiency. Bone mineral densities in the lumbar spine and the femoral neck were normal. Bone Scintigraphy and tumour marques levels were normal. Patient underwent an orthopedics treatment with lumbar orthosis and bed rest for 2 months; radiographic control 3 months later demonstrated good respect of lumbar lordosis.

Conclusions:: CONCLUSION Seizure-induced vertebral fracture has been recognized, but has rarely been reported in the neurosurgical literature. A complaint of back pain after a convulsive seizure should prompt radiologic investigation for vertebral fracture, even in the absence of external trauma.
INTAKES OF FATTY ACIDS WITH ANTI-INFLAMMATORY PROPERTIES AND SEIZURE OUTCOMES IN A POPULATION OF EPILEPTIC PATIENTS FOLLOWING A GENERAL DIET

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Background and Aims:: Some evidence suggests individual fatty acids may elicit anti-seizure effects in patients unable to follow a ketogenic diet. We aimed to measure intakes of fatty acids with anti-inflammatory properties and determine the associations between those intakes and seizure outcomes in epileptic patients following a general diet.

Methods:: In a prospective cohort of patients admitted to an Epilepsy Monitoring Unit, seizure activity was monitored via continuous video electroencephalogram and seizure presence and severity was quantified. Dietary intake was determined via a food frequency questionnaire. A Mann-Whitney U test was used to compare median fatty acid intakes between groups of seizure activity. Linear and logistic regression models were used to analyze relationships between fatty acid intake and seizure presence and severity.

Results:: 82 participants were included. Overall intake of omega-3 was below recommended levels; intakes of saturated fat were high. Median intakes of short- and medium-chain saturated fatty acids were borderline statistically significant between groups, with the seizure presence group having higher intakes of both (0.65 gm vs. 1.01 gm for no vs. yes seizure presence, p = 0.07 and 2.92 gm vs. 3.82 gm for no vs. yes seizure presence, p = 0.07 for short-chain and medium-chain, respectively). Regression models did not identify any fatty acid as a predictor of seizure presence or severity.

Conclusions:: Patients with epilepsy who are not following a ketogenic diet consume diets that may adversely impact seizures. Further research in this population is warranted.
A STUDY OF SEIZURE RISK FACTORS IN CHILDREN WITH GASTROENTERITIS ADMITTED IN WEST BENGAL PEDIATRIC'S HOSPITALS

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Background and Aims:: Based on attention to the high prevalence of G/E in children and their complications like seizure we must research about the reasons and predisposing factors of it to find out the main reasons of the complications. G/E and seizure are important etiologies of mortality and morbidity in children, specially in children under 6 year old. Our aim was to determine the predisposing factors of convulsion in children having diarrhea hospitalized in West Bengal Hospitals through 2017-2019.

Methods:: In this case-control study we compared predisposing factors of convulsion in 507 children with diarrhea and convulsion in West Bengal pediatric hospitals. Age of children in two groups were between 1 month- 15 years. Risk factors in seizure for example age – leukocytosis... were studied in the research. Our study results statistically analyzed with Chi-square test.

Results:: In this study from 570 patients with G/E and convulsion 310 patients were males and 260 patients were females. In control group 310 patients were males and 26 patients were females that were under 3 years old, especially between 1 months–15 year old. 91 of patients were under 12 year old. 12.3% patients had positive familial history for convulsion. In this study most common types of seizure were generalized. More seizures had happened before the hospitalization. 94.2% of seizures had duration of lower than 15 minutes. The mostly dehydration was medium and most clinical manifestation was fever in two groups.

Conclusions:: This study detected predisposing factors for convulsion in G/E patients were lower age, positive familial history for seizure and leukopenia.
CONSENSUS FOR THE CLINICAL UTILITY OF BIVARACETAM IN INDIAN PATIENTS - SURVEY RESULTS OF THE INCLUDE COLLABORATIVE GROUP

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Background and Aims:: We conducted a nationwide perception mapping exercise to understand and draw consensus for clinical utility of brivaracetam in everyday clinical practice

Methods:: 317 thought leaders in neurology were invited through whatsapp and email, to respond to a structured questionnaire, developed through a customised technological virtual response system from March 24-April 30, 2021. Anonymised data were analysed by using GraphPad software version 8.4.3

Results:: Mean experience, across 250 respondents, was 13 years (SD 9.3, 95% CI 11-14). Cumulative man-years experience was 3128 years. Amongst the Newer Antiepileptic Drugs (AEDs), 43.6 % (n=109), 49.6% (n=124), 36.8% (n=92), 34% (n=85) ranked brivaracetam as the most preferred for safety, ease of titration, efficacy, potential as an efficacious monotherapy agent, respectively. Brivaracetam has a wide therapeutic window, for higher completion rates for higher doses and its higher level of evidence has created impact for the reason to choose brivaracetam was agreed/ strongly agreed by 86.8% (n=217) and 94.4 % (n=236), respectively. The patients in whom brivaracetam is initiated, 71.6% (n=179), reported that they are already on 1-2 AEDs and the duration of epilepsy is less than 10 years as reported by 84.4 % (n=211). Favorable tolerability was the most important reason for the choice for brivaracetam in Indian patients with uncontrolled focal epilepsy by 63.2 % (n=158). 88 % (n=220) opined that patients were satisfied with brivaracetam

Conclusions:: Virtual expert nation-wide consensus mapping exercise revealed favorable agreement for utilization of brivaracetam in Indian patients which is in concurrence with the emerging evidence for its favorable tolerability and efficacy
Background and Aims:: Introduction 20-40% of patients with epilepsy, have refractory epilepsy (ER) defined as the failure of the use of two tolerated oral antiepileptic drugs, suitably chosen to achieve sustained crisis control. Objective Describe the characteristics of patients submitted to the refractory epilepsy surgery protocol (PCER).

Methods:: Materials and methods Longitudinal descriptive observational study of patients undergoing PCER and surgically treated; description of general characteristics, differences before and after 8 months of quality of life, disability and frequency of crisis.

Results:: Results We reviewed 103 patients, female (57.8%), mean age 24 years, mean time of evolution of epilepsy 15.91 years; complete baccalaureate level of education (20.4%); history of prematurity, fetal distress and neuroinfection (33.9%), family nexus of epilepsy (34.9%); start with focal crisis (80.6%); mild mental deficit in neuropsychological evaluation (37.9%); The most common finding in MRI was left hippocampal sclerosis (27.1%); video-electroencephalographic monitoring with left temporal discharge (24.3%); FAES most prescribed carbamazepine and valproic acid. The main behavior was neurosurgical (69.9%) and total callosotomy the most performed procedure (30.6%). At 8 months after surgery, significant favorable changes were found (p <0.05) in number of seizures, quality of life measured by CAVE in children and adolescents, and QOLIE-10 in adults. No significant changes were observed in the Barthel scale of disability.

Conclusions:: Discussion and Conclusions The results support a significant positive impact in the patients who undergo surgery. Additional studies are required over time, which allow for improvements in the results of disability and medication use, as well as additional safety elements.
EPILEPSY CONTROL WITH CARBAMAZEPINE MONOTHERAPY FROM A GENETIC PERSPECTIVE

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Background and Aims:: Ethnicity variation is one of the main factors that may affect drug response in clinical practice. As MTHFR gene affects different transcriptome and proteome which affect the clinical response of drugs. Purpose of the current study was to observe possible variations in plasma levels of carbamazepine monotherapy and seizures’ control in Pakhtun population of Khyber Pakhtunkhwa (KP) in the context of MTHFR (C677T and A1298C) gene polymorphisms.

Methods:: Blood was collected from the epileptic patients treated with carbamazepine monotherapy for the first time following respective oral doses on its steady state concentration after 3 h of morning dose at 3rd and 6th month of the therapy. Plasma carbamazepine levels were determined using reverse phase high performance liquid chromatography after method validation. MTHFR (C677T, AA298C) gene was genotyped. Patients were followed on 3rd and 6th month of the therapy for monitoring of response to carbamazepine therapy.

Results:: Following for 3rd and 6th month of duration of carbamazepine therapy, poor seizure controlled patients were more likely noticed in heterozygous variants (677CT and 1298 AC) of MTHFR gene (P < 0.05). There was no significant (P > 0.05) difference in the dose and plasma level of carbamazepine among different genotypes of MTHFR (C677T and A1298C) gene. Similarly, the difference in dose and plasma level of carbamazepine was not significant (P > 0.05) in the responder and non-responder people with epilepsy.

Conclusions:: heterozygous variants of MTHFR (C677T and A1298C) gene are associated with poor seizure control in Pakhtun population of KP.
INFLUENCE OF WRIST TAPPING ON ALPHA RHYTHM SYNCHRONIZATION IN HEALTHY ADULTS AND ADULTS WITH JUVENILE MYOCLONIC EPILEPSY

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Background and Aims:: Background: The aim of this study was to assess the effect of wrist tapping (WT), according to the author's method, on the synchronization of alpha activity in healthy adults and patients with juvenile myoclonic epilepsy (JME).
Methods:: The study included 71 people of working age, including 51 clinically healthy volunteers (median age – 39 [21;56] years) and 20 patients with JME (median age 27 [23;35] years)
Results:: In JME patients, there were statistically significant changes in the alpha peak frequency (P<0.05) and alpha power (P<0.05), as well as a statistically significant increase in the the alpha range width (P<0.05) after WT. WT, according to the author’s technique, allows reducing the severity of alpha rhythm synchronization and leads to a shift in the peak frequency of the alpha rhythm in the occipital leads towards the alpha-2 sub-frequency range and a decrease in AP in both healthy volunteers and JME patients. At the same time, the alpha range width in the occipital leads is statistically significantly increased in JME patients.
Conclusions:: The nature of the change in the alpha rhythm, in comparison with the control, indicates the phenomenon of resonance with the frequency of the WT rhythm. The WT effect testifies to the prospects of the clinical application of WT in JME, since it was previously shown that if the selected external frequencies enter into resonance with the neurons of the antiepileptic system, then an antiepileptic effect could be obtained.
LATERALISATION OF PAROXYSMAL ACTIVITY AND ALEXITHYMIA IN EPILEPTIC PATIENTS

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Background and Aims:: Background. In recent years, data have appeared on the relationship of alexithymia with cerebral deficiency and functional interhemispheric asymmetry. Aim. To study the relationship between paroxysmal activity (PA) and alexithymia in patients with epilepsy.

Methods:: The study involved 45 patients with epilepsy from 18 to 59 years: men 45% (N=20), women 55% (N=25). 3 groups were distinguished: 1 - PA in the left hemisphere (N=17); 2 - PA in the right hemisphere (N=9); 3 - without a predominant lateral accent PA (N=6). The level of alexithymia was determined by Toronto Alexithymic Scale (TAS). The data were processed by the SPSS 16.0.

Results:: There are 38% patients with alexithymia (N=17), 40% patients in zone of uncertainty (N=18), 22% patients without alexithymia (N=10) in the total sample. 1 group – 75±12.3 points; 2 group – 77±16.4 points; 3 group – 61±15.6 points (without alexithymia) by TAS. Significant differences were found in the level of alexithymia only between 2 and 3 groups (p = 0.002). 2 group patients, in contrast to the rest, had difficulties in identifying and describing feelings and an external type of thinking (p = 0.004, p = 0.001).

Conclusions:: Patients with epilepsy and alexithymia have cognitive features: a slowdown in the rate of mental performance, difficulty switching attention, specific situational way of thinking, and a decrease in communication capabilities. The level of alexithymia is more pronounced in epilepsy with paroxysmal activity in the right hemisphere. The results can be applied in the process of treatment and rehabilitation of patients with epilepsy.
DRUG AND SUBSTANCE ABUSE IN REFRACTORY EPILEPSY

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Background and Aims:: Seizures often occur in substance abusers. The aim of the present work; is to study the etiology of non-response to antiepileptic drugs by estimating their serum levels and screening of drugs and substance abuse in patients with resistant epilepsy.

Methods:: this study was conducted in epilepsy outpatient clinic, neurology department, Mansoura University Hospital. After exclusion those with organic brain lesion and who were not compliant to antiepileptic treatment, 924 patients with intractable epilepsy were included. They were subjected to: - Toxicology screen for detection of drug and substances abuse by analysis of urine and blood samples. - Measurements of the level of antiepileptic drugs in the blood (carbamazepine, valproic acid, phenytoin). All assays run on the system use of homogenous immunoassay technique EMIT (Enzyme Multiplied Immunoassay Test) and confirmed by GC/MS (gas Chromatography/Mass Spectrum).

Results:: Confirmed Positive results for drugs and substances abuse were detected in 246 of 924 patients (26.62%) by GC/MS. Cannabis was the first abused drug (29.27%), opiates was the second drug abused by patients (21.95%) followed by alcohol (17.88%), benzodiazepine (16.26%) tricyclic antidepressants (8.54%) and finally barbiturate constituted (6.1%). Only 17 patients show serum level of antiepileptic drugs (carbamazepine, valproate and phenytoin) within therapeutic range, but 169 patients’ levels were below it and 60 patients with levels above it.

Conclusions:: Substances abuse may be the cause of resistant epilepsy as they are epileptogenic by themselves or due to drug-drug interaction with the antiepileptic.
PSYCHOMETRIC PROPERTIES OF THE RUSSIAN LANGUAGE VERSION OF THE GAD-7 IN PATIENTS WITH EPILEPSY.

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Background and Aims:: Patients with epilepsy (PWE) are at higher risk of developing an anxiety disorder than the general population. The prevalence rate of generalized anxiety disorder (GAD) in PWE is about 10% (Scott et al., 2017). The Generalized Anxiety Disorder-7 (GAD-7) has been translated into numerous languages, and some versions were found to be a valid screening tool for detecting GAD in PWE. However, the screening properties of the Russian version of the GAD-7 in PWE have not been investigated yet. We aimed to investigate the Russian version of GAD-7 as a GAD screening tool in PWE.

Methods:: A consecutive PWE cohort was assessed with GAD Module of the Mini International Neuropsychiatric Interview (MINI) and the GAD-7. Demographic and clinical variables were collected. Receiver operating characteristic (ROC) analyses for GAD-7 scores, with higher Youden’s index identification, were used as statistical methods.

Results:: The cohort consisted of 233 PWE: 152 (65.4%) female; mean age was 41.1 (14.7); 213 (91.4%) had focal epilepsy; mean age at onset of the epilepsy was 24.8 (16.8), 61 (27.5%) had GAD. ROC analysis showed an area under the curve of 0.922 (95%CI 0.879-0.964). At the cutoff point >9 GAD-7 had a sensitivity of 96.6% (95%CI 80.7-96.5), a specificity of 88.7% (95% CI 83.0-93.1), a positive predictive value of 49.4% (95%CI 38.8%-60.0), a negative predictive value of 98.8 (95% CI 97.3-99.4)

Conclusions:: The GAD-7 was found to be an effective, reliable and valid screening tool for detecting GAD in PWE.
Background and Aims:: A prevalence rate of depression in persons with epilepsy (PWE) is higher than in the general population and ranges between 13-36% (Fiest KM et al., 2013). Depression in PWE is often underrecognized because of the lack of valid screening tools for this population. The depressive subscale of the Hospital Anxiety and Depression Scale (HADS-D) might be a useful screening tool for major depressive disorder (MDD), but the Russian language version has not been validated in PWE yet. We aimed to investigate the Russian language version of HADS-D as MDD screening tool in PWE.

Methods:: A consecutive cohort of PWE was assessed with the current major depressive episode module of the Mini International Neuropsychiatric Interview (MINI) and the HADS-D. Demographic and clinical variables were collected. Receiver operating characteristic (ROC) analyses for HADS-D scores, with the higher Youden's index identification, were used as statistical methods.

Results:: The cohort consisted of 175 PWE: 119 (68%) were female; mean age 41.5 (15.9); 160 (91.4%) had focal epilepsy; mean duration of epilepsy 14.33 (12.7) years, 99 (56.5%) had current MDD. The ROC analysis showed an area under the curve of 0.854 (95%CI 0.793-0.903). At the cutoff point >7 HADS-D had a sensitivity of 69.7% (95%CI 58.1-79.8), a specificity of 83.8% (95% CI 75.1-90.5), a positive predictive value of 56.4% (95%CI 44.7-67.5), and a negative predictive value of 90.2 (95% CI 86.6-92.9).

Conclusions:: Validity of HADS-D for detecting MDD in PWE is questioned by its modest sensitivity.
IMPACT OF COVID-19 PANDEMIC ON RURAL SOUTHERN INDIAN EPILEPTIC PATIENTS

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Background and Aims:: Background: During Covid-19 Pandemic, seizure control may worsen. During the Covid-19 Pandemic, Collateral damage may occur in epileptic management. This study was aimed to establish the impact of this covid-19 Pandemic on epileptic patients in terms of seizure control and emergency problems.

Methods:: Material and methods: This is a cross sectional study carried out in my epileptic Patients at ABC Hospital Trichy, Dhanlaxmi Srinivasan Medical College Hospital and KM Crescent Hospital. Epileptic Patients were assessed by telephonic contact during the lockdown period of 100 days at the central part of Tamilnadu in Southern India. Datas regarding the impact of lockdown economic effects of the Pandemic, AEDs availabilities, drug compliances, Seizure triggers, and the subjective perception of teleconsultation were recorded and analysed.

Results:: - Three hundred and sixty six patients were taken up for this study. Among them 266(72.67) were male and 100(27.32%) were female. AEDs were available for all the Patients. But regular specific brand of AEDs are Substituted in 293(80.05%) patients. Breakthrough seizures were recorded in 168 (45.90%) Reduction in Income were noted in 296(80.87%) patients during this pandemic. Teleconsultation were considered useful in 32 % of the epileptic patients during the lockdown.

Conclusions:: Conclusion: - The current covid-19 pandemic definitely has effects in the rural epileptic patients. Change of AED’s brand, skipping of AEDs, stress, sleep loss and economic difficulties are the risk factors for the increased seizure frequency. Teleconsultation awareness is less in rural population. A significant percentage of patients with epilepsy (PWE) had experienced difficulties in followup.
COMMUNITY AWARENESS OF WHICH SEIZURE TYPES SHOULD PRESENT TO HEALTHCARE PROVIDERS; A POTENTIAL RISK FACTOR OF EPILEPSY TREATMENT GAP

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Background and Aims:: The objective of this study was to assess the awareness of the highly educated community of which seizure type(s) should present to health care providers

Methods:: This is a cross-sectional descriptive internet based survey that was conducted in Sudan during the period from January to April 2018, using google forms. The survey consisted of demographic data (age, gender, educational level), a statement evaluating participants' sources of obtaining information regarding epilepsy, a statement assessing awareness about the primary care provider for people with epilepsy (PWE), and a statement describing the symptomatology of different seizure types in simple Arabic, asking what description(s) participants thought should present to health care providers. We included participants residing in Sudan, and those with college degree or higher education. Four hundred sixty seven participants completed the survey

Results:: 467 participants were included, of whom, 279 (60%) were females. The mean age of participants was 28 years. Two thirds of participants obtained their information from nonscientific sources. 84% of the participants were aware that doctors are the primary health care providers for people with epilepsy.

Conclusions:: this study demonstrated poor awareness about the necessity of presentation for focal and absence seizures. We hypothesize that this lack of awareness may contribute to epilepsy treatment gap, and we recommend further studies to examine this hypothesis.
« PEHO SYNDROME: A STUDY OF TWO (2) PATIENTS OBSERVED AT THE ACADEMIC HOSPITAL IN CONAKRY”

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Background and Aims:: le but de faire une réévaluation de cette pathologie à partir du plan clinique, électrochimique et point de vue neuroradiologique. L'intérêt de ce travail réside dans le fait que ces observations illustrent les encéphalopathies en général et leurs difficultés diagnostiques comme présen

Methods:: L'intérêt de ce travail réside dans le fait que ces observations illustrent les encéphalopathies en général et leurs difficultés diagnostiques qu'elles présentent en milieu tropical en particulier.

Results:: We report two sporadic cases of PEHO (Progressive Encephalopathy with oedema, hypsarrhythmia, and Optic atrophy) which meet the electroclinical and neuroradiological criteria of the disease. In our knowledge, these cases are the first to be described in a Sub-Saharan African (SSA) country, a review of the literature through these two cases, with the aim of making a re-evaluation of this pathology from the clinical, electrochemical and neuroradiological point of view.

Conclusions:: Conclusion: the PEHO in the African environment is real and shows the difficulties of management which deserve the attention of pediatricians and neuro-pediatricians given the rarity of this syndrome.
Background and Aims:: Nihilistic views are sometimes expressed that finding a genetic cause does not alter management, and therefore genetic testing is unnecessary. It is underused in cases of epilepsy and wise use of genetic testing can improve outcomes in refractory epilepsy. We describe 4 cases paediatric refractory epilepsy in which genetics changed the management and prognosis.

Methods:: Case 1: 7/F born of nonconsanguineous marriage presented with absence seizures 100–200/d, head drop & occasional falls on 4 AEDs since 2 years of age. She had mild developmental delay, poor scholastic performance, microcephaly, lower limb spasticity. Case 2: 6/F, born of 2nd degree consanguineous marriage, falls 100-150/d, touch & sound sensitive myoclonic jerks on 5 AEDs Case 3: 7/M, Normal birth & developmental history Refractory right & left focal seizure with severe language & social decline. Partial response to IVIG and steroids, developed steroid toxicity Case 4: 18/M born of a consanguineous marriage, presented with clinical features of cerebellar ataxia, early cataracts, neuropathy, sub normal IQ and seizures

Results:: Analysis of these all 4 patients charted in following pictures
**Conclusions:** In absence of structural lesion, refractory seizures should prompt the physician to consider potentially treatable metabolic epilepsies, especially in poor scholastic performance. Suspect GLUT 1 deficiency in atypical and late onset presentations of refractory absences with/without movement disorders. Not all cases with myoclonic jerks are PME. Hyperekplexia should be kept as one of differentials. Long term cost of therapy and quality of life greatly outweighs cost of testing.
LOCALIZATION OF ICTAL ISLAMIC RITUALS: STUDY FROM EPILEPSY CENTER IN MAKKAH

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Background and Aims:: Ictal semiology is important to aid the diagnosis of seizure type. Patients frequently requires admission to Epilepsy monitoring unit (EMU) in order to reach a correct diagnosis of epilepsy type. Some patients may exhibit unusual ictal phenomena that sometime lead to the diagnosis of psychogenic seizure. Some of unusual ictal phenomena are ictal kissing, praying and drinking. Ictal religious speech and praying are examples of the unusual ictal phenomena. The aim of this study is to assess the localization value of ictal Islamic rituals.

Methods:: We retrospectively reviewed all patients admitted to epilepsy monitoring unit at King Abdullah Medical City in Makkah between 2017 to 2021. Patients with ictal Islamic rituals were included in the study.

Results:: Nine out of 279 cases admitted to EMU have different ictal Islamic rituals. Two patients had hand automatism mimicking Islamic prayer. Four patients have Islamic religious speech including calling Allah to help, asking for forgiveness, and praying. Three patients exhibited fortification. All nine patients had seizure originating from the right temporal lobe.

Conclusions:: Islamic rituals are rare ictal phenomena that localized to right temporal lobe.
POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME. ABOUT 5 CASES

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Background and Aims:: We herein present five case reports discussing the clinical and pathogenesis aspects of posterior reversible encephalopathy and the place of imagery in its management.

Methods:: We report the case of five patients, the first followed for systemic lupus erythematosus, the second is hypertensive poorly follow-up, the 3 other patients were in postpartum after cesarean delivery. All our patients had generalized tonic-clonic seizures associated with an hypertensive peak without edema syndrome.

Results:: Laboratory tests were unremarkable. The EEG showed epileptic abnormalities and brain MRI was in favor of a reversible posterior leukoencephalopathy.

Conclusions:: The PRE is an unusual neurological complication of post-partum with vasogenic edema by disrupting the blood-brain barrier (BBB) seems to be the main actor. The initial clinical presentation is variable, ranging from simple headaches to dramatic presentations of status epilepticus. The DWI MRI is the best diagnostic tool enabling rapid and appropriate treatment to prevent the occurrence of irreversible neurological damage and permanent sequelae.
INCIDENCE OF POST TRAUMATIC EPILEPSY IN KHARTOUM STATE, SUDAN BETWEEN THE PERIOD OF DECEMBER 2018 TO JANUARY 2020

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Background and Aims:: Epilepsy is one of the commonest neurological disorders. It has a strong association with trauma to the brain, constituting of 5% of epilepsy cases. To determine the prevalence of post-traumatic epilepsy among Sudanese patients and to demonstrate the relation between traumatic brain injury and occurrence of epilepsy.

Methods:: A descriptive hospital-based cross-sectional study, conducted in Bashiar, Omdurman, and Ibrahim Malik Teaching Hospitals in Khartoum state, in the period from December 2018 to January 2020. Patients were interviewed by general emergency team. Relevant history was obtained, and both biochemical and neuroimaging investigations were done.

Results:: 70 patients with history of traumatic brain injury (TBI), 6 (11.3%) developed post traumatic epilepsy (PTE). (82.9%) were males and (17.1%) were females. In the 6 patients who developed PTE, the mode of trauma in two of them was gunshots, two due to fall, one by an automobile accident and one had missing data. Out of them, one had subarachnoid hemorrhage, one had bilateral subdural hematoma and one developed massive epidural hemorrhage. Statistically significant correlation was found between TBI and number of comorbid conditions. Older age was associated with more severe TBI. Significant correlation reported between the etiology of TBI and occurrence of PTE. Significant correlation between higher GCS at the time of trauma and not having PTE. People with TBI and GCS more than 12 had 1.8 less chance to develop PTE.

Conclusions:: Traumatic brain injury constituting of type of trauma, etiology, formed of brain injury, and GCS at presentation, has a significant implications to occurrence of epilepsy.
THE LONG-TERM EFFECTS OF TERATOGENIC INFLUENCE DURING THE PREGNANCY ON COGNITIVE DEVELOPMENT OF A CHILD IN CASE OF MOTHER'S EPILEPSIA.

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Background and Aims:: Epilepsy is a severe stigmatizing disease that affects all areas of the patient's life and limits his social and individual opportunities and rights. Until recently, the birth of a child was often a pipe dream for women suffering from epilepsy, since high risks of cognitive violations. We claim, that with due responsibility it is possible to raise a healthy child, but we have to assess all the risks, which is our study aimed for.

Methods:: 80 people: 40 mothers with epilepsy and 40 children aged 3 to 9 years. We used Wechsler WSIC Intelligence Scale for Children and the Luria Battery of Neuropsychological Tests adaptated by J.M. Glozman, and several methods for observing child's behaviour. Data on the clinical condition of the mother during pregnancy and childbirth were also collected.

Results:: The study showed that intellectual development of children is affected by the form of mother's epilepsy, antiepileptic drugs taken by her, preparedness of childbirth, the presence of seizures during pregnancy, complications of pregnancy, the way of parturition and the type of feeding. The most important factors for reducing the impact of teratogenic effects were the preparedness of the birth, the absence of seizures during pregnancy and the absence of complications of pregnancy.

Conclusions:: It can be confirmed that teratogenic effects have a significant influence on the cognitive development of a child, but studying structure of these effects allows us to plan pregnancy as safe as possible for both the patient and the fetus.
THE PROBABILITY OF THE EPILEPSY IN CHILDREN AFTER THE SINGLE SEIZURE

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Background and Aims:: The diagnosis of epilepsy can be made based on a single seizure. Probability and time of recurrence of attack at different age periods not sufficiently studied.

Methods:: Case-control study. 556 children after a single seizure are included in a prospective two-year study. Five subgroups were formed on the age of the children at which the first attack occurred: up to 1 y.o. (n=202); 1-3 y.o. (n=134), 4-5 y.o. (n=45); 6-13 y.o. (n=133); 14-17 y.o. (n=42).

Results:: Two groups were formed: the 1st group (n=447) with a recurrent attack (epilepsy), the 2nd group (n=109) with only a single seizure. In the total cohort (n=556) the likelihood of a seizure recurrence is 0.799 (95%CI [0.762; 0.829]) 12 months after the first seizure; 0.804 (95%CI [0.768; 0.834]) 18 months after the first attack and remains approximately at this level until the end of the two years. The maximum increase in the likelihood of re-attack was in the first 3 months after the first attack: 0.700 (95%CI [0.659; 0.735]). The probability of developing a second attack in the age subgroups varies significantly (p log rank<0.001), the maximum likelihood of a recurrence of an attack occurs in children with the first attack before the age of 1 y.o. In this subgroup the probability is 0.856 (95%CI [0.799; 0.897]) 1 month after the first attack and 0.916 (95%CI [0.867; 0.947]) in 3 months.

Conclusions:: The results of the study make it possible to prognosis the relapse of the first seizure in children for their management improving.
IS INTELLECTUAL DISABILITY RELATED TO POOR CONTROL OF EPILEPSY? OMDURMAN, SUDAN (2020-2021)

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Background and Aims:: Epilepsy is one of the commonest neurological disorders. It has a well-known recognized association with intellectual disabilities. To assess the relation between intellectual disability and epilepsy control.

Methods:: This is a descriptive institutional-based cross-sectional study that was conducted in Daoud Research Group Charity clinic in sudan, during the period (November 2020-January 2021). A total of 34 patients with intellectual disabilities and epilepsy where included in this study. The IQ test, full history, relevant clinical examination and specific investigations were done.

Results:: Out of 34 patients, 26 were males (76.5%) and 8 were females (23.5%), age ranged from 2 to 35 years, with mean age 17 years. 25 of the participants (73.52%) have intellectual disability of unknown cause, 3 of them have Wilson disease (8.82%), 2 have meningitis (5.88%), while fragile-X syndrome, encephalitis, cerebral palsy and infantile hemiplegia accounted for 1 patient each (11.76%). 19 of the participants have generalized tonic-clonic epilepsy (55.88%), 7 have focal to bilateral (20.58%), 4 have focal with impairment (11.76%), 1 has focal without impairment (2.94%) and 2 have atonic epilepsy (5.88%). Most of the participants had high seizures frequency (76%), minority had low frequency (8%), and a middle frequency (16%). We also found that the majority of the patients had no period fits free(61%), whereas 23% of the patients had a less than one year fits free, and 16% of them had maximum a period free of fits of 1 to 2 years.

Conclusions:: Intellectual disability has a strong association with poor control of epilepsy.
PREVALENCE AND RISK FACTORS OF PSYCHOCENIC NON-EPILEPTIC SEIZURES AMONG ADULT SUDANESE EPILEPTIC PATIENTS WHO ATTEND DAOUD CHARITY CLINIC, KHARTOUM, SUDAN 2021

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Background and Aims:: Seizures can present in many diseases such as epilepsy which is one of the common neurological disorders. Some seizures can present as psychogenic seizures. Epilepsy can be associated with psychogenic non-epileptic seizures. To assess prevalence and risk factors of psychogenic non-epileptic seizures among adult Sudanese epileptic patients attending Daoud charity clinic.

Methods:: A descriptive cross-sectional facility based study was conducted during Jan-Feb 2021. Data collection was done via interview based structured questionnaire and a total number of 99 participants were included in the study.

Results:: Overall 99 adult epileptic patients were included. 57% were females, the majority of patients reside inside Khartoum (79%) and reach secondary schools (32%). The main type of epilepsy was generalized tonic clonic (68%) followed by focal with impairment (11%). The majority of patients have been diagnosed as epilepsy for more than three years (65%). 29 patients (29%) had a history of psychogenic non-epileptic seizure. The prevalence of psychogenic non-epileptic seizure was found to be significantly higher in patients with social problem and/or depression (p value 0.005, 0.00 respectively). Patients with depression were 14 times more likely to have psychogenic non-epileptic seizures (CI 95%: ##-##). Most of participants have no history of sexual abuse, physical abuse or school/University/work refusal and/or absence (94%,84% and 63% respectively).

Conclusions:: A considerable high prevalence rate of psychogenic non-epileptic seizures can be found among adult epileptic patients . Epileptic patients suffering from social problems, and/or depression are more vulnerable to develop psychogenic non-epileptic seizures especially during the last two years of treatment or above.
STUDY OF KNOWLEDGE ATTITUDE AND PRACTICE TOWARD EPILEPSY AMONG PARENTS AND CARE GIVERS OF CHILDREN WITH EPILEPSY SEEN IN FATHALRAHMAN ELBASHIR CLINIC, KHARTOUM 2019-2020

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Background and Aims:: Epilepsy is one of the most common pediatric neurological disorders. Lack of awareness regarding epilepsy among the general population influences the lives of epileptic children. The aim of this study was to assess the knowledge, attitude and practice toward epilepsy in parents and care givers of children with epilepsy in FathElrahman Elbashir clinic.

Methods:: 120 parents and care givers were included in the Case finding study conducted at FathElrahman Albashir clinic, Khartoum from (September 2019 - January 2020). An interviewing questionnaire was designed to collect data from the participant families.

Results:: Total of 120 parents and care givers were interviewed. 48.3% were mothers, the age of children ranged from 1-18 years. 41.7%, believed that epilepsy is caused by evil eye. About 85% said epilepsy is curable disease. 91.6% think the best treatment is antiepileptic drugs, but 51.6% still believed in nonmedical treatment usually traditional helps and 100% use holy Quran as a method of religious treatment for epilepsy.

Conclusions:: Many parents and care givers have significant misconceptions, negative attitudes, and poor practices toward epilepsy. These correlated with their educational levels and had significant implications on the medical management. Level of knowledge and understanding among parents and care givers of children with epilepsy needs improvement.
LANDAU-KLEFFNER SYNDROME: A 17-YEAR FOLLOW-UP WITH ATYPICAL OUTCOME

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Background and Aims:: Landau-Kleffner syndrome (LKS) is a rare entity characterized by epilepsy and afasia, whose outcome is variable, usually initiating between three to seven years old. The aim of this case is to describe a follow-up for 17 years of a patient with LKS.

Methods:: This case report was written based on data of the medical record of a 21 year-old male patient, accompanied since four years old due to LKS.

Results:: Subject started, at the age of four, with abrupt aphasia, although there wasn’t reports of seizures. The electroencephalogram showed temporal and parietal epileptiform discharges, during NREM sleep. Brain CT with cerebral perfusion demonstrated moderate hypoperfusion in the right medial frontal lobe, mild in the left, in addition to mild hypoperfusion in medial temporal lobe in both hemispheres. He was treated with carbamazepine, valproate, clonazepam and oral corticosteroids, but the progressive improvement occurred after the beginning of sulthiame at six years old. Currently, the patient remains stable, with good communication and social interaction, without new events, attending higher education, with an intelligence quotient of 117.

Conclusions:: LKS is a heterogeneous entity. It is known that the electroencephalogram findings tend to improve as around 15 years of age, while the long term prognosis of afasia remains poor, probably due to the early age of onset, which is the most limiting factor for a low psychosocial result. This case evidenced a long-term follow-up of a patient with Landau-Kleffner syndrome, with a favorable outcome in speech and cognition, unusually seen in the literature.
SLOW TAPERING OF ANTI-EPILEPTIC DRUGS VERSUS RAPID TAPERING AMONG SUDANESE EPILEPTIC PATIENTS ATTENDING DAOUD CHARITY CLINIC, KHARTOUM, SUDAN 2019-2020

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Background and Aims:: Treatment of epilepsy should be for at least two years. After successful treatment, the drug withdrawal should be gradual. This study aimed to study the rapid versus slow withdrawal of antiepileptic drugs in Daoud charity clinic in the period between January 2019 to January 2020.

Methods:: A descriptive cross-sectional, clinic-based study. A total of 32 epileptic patients who had already undergone tapering were included. Data collection was via a structured questionnaire by a neurology consultant. Patients were dividing into two groups, the slow withdrawal group was considered in more than 3 months, while the rapid withdrawal in less than 3 months.

Results:: 14 patients (43.8%) underwent rapid tapering and 18 patients (58.3%) underwent slow tapering. 53.1% were males and 46.9% were females. The majority had a generalized tonic-clonic (62.5%) followed by complex partial (15.6%). Sodium valproate users were 66%, while carbamazepine ones were 33%. The most common trigger factors for epileptic fits were infections (46.9%). Among 32 patients, 25% had abnormal MRI while 41% had abnormal EEG. The most common type of seizure after relapse was generalized tonic-clonic (65.6%) followed by complex partial (15.6%). The recurrence rate of epilepsy was found to be higher in rapid tapering (12.5%) in the first three weeks compared to slow tapering (6%). A higher rate of reoccurrence in the first year was for slow tapering (40.6%) compared with rapid tapering (34.4%).

Conclusions:: The recurrence of rapid withdrawal in short term was higher and regarding slow withdrawal, the recurrence was higher in the long term.
PATTERNS OF CLINICAL PRESENTATION OF EPILEPSY AMONG ADULT SUDANESE EPILEPTIC PATIENTS SEEN IN SINGA SUDAN A RURAL AREA STUDY EXPERIENCE

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Background and Aims:: Epilepsy is one of the commonest neurological disorders in which brain activity becomes abnormal, causing seizure and periods of abnormal behavior, sensation, and sometimes loss of awareness. The study aims to study the Patterns of clinical presentations of epilepsy among adult Sudanese epileptic patients seen in singa rural Sudan.

Methods:: A prospective cross-sectional study was conducted at Daoud mobile charity clinic in singa Sudan on 13 November 2020. 40 Patients with epilepsy were included in this study. Full detailed history and proper clinical examination were done for each patient.

Results:: Out of 40 patients 21 (52.5%) were females and 19 (47.5%) were males. Age of the patients ranged from 20 to 70 years, 20-30 year was found to be the most common age group (62.5%). 32 patients (80%) had generalized epilepsy. We found that most of the patients had a higher seizure frequency per month (62%). The prodromal and neurological sings were found just in (32.5%) of the patients. Fever was found to be the most seizure provoked factor (35%). 14 patients (35%) with well controlled epilepsy While 26 patients (65%) were poor controlled. There is strong relation between type of medication and increase frequency of attack convolution. Carbamazepine was the most common drug used among the patients that have been seen in singa rural Sudan, followed by sodium valproate, lamotrigine and levetiracetame.

Conclusions:: Generalized epilepsy is the most common type of epilepsy. Patients who live in the singa (a rural Sudan area) have a poor controlled epilepsy.
EPILEPSY SURGERY; WHEN THE EPILEPTOGENIC ZONE CORRESPONDS WITH THE SUPPOSED WERNICKE’S AREA

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Background and Aims:: An epileptogenic lesion in highly eloquent cerebral areas does not necessarily contraindicate epilepsy surgery, but it may require further diagnostic procedures, also invasive. If a language area is involved, functional study is greatly complex.

Methods:: Woman 26 years old, right handed. Drug-resistant seizures from the age of 7, characterized subjectively by a shiver on the right side of the body, then auditory hallucinations from the right ear; objectively patient incapable to verbally warn of the arrival of the seizure, then psychomotor arrest without automatisms or dystonic postures. At the end a language disturbance was not clearly definable. Seizures with brief duration, weekly. Brain MRI revealed a left mid-posterior superior temporal gyrus (STG) blurring of the gray-white matter junction, consistent with focal cortical dysplasia type II (FCD). fMRI for language showed a bilateral activation for comprehension and a left activation for fluency. Interictal EEG demonstrated left temporal spikes and polyspikes and waves with rhythmic and subcontinuous occurrence during sleep.

Results:: A left temporal-perisylvian Stereo-EEG was performed, with two electrodes exploring the right STG. Spontaneous seizures were recorded, with onset from the FCD. Intracerebral stimulations were crucial in determining a right lateralisation of Wernicke’s area. Stereo-EEG-guided radiofrequency thermocoagulations in the left mid-posterior STG were performed, without complications. Patient is seizure free (short follow-up).

Conclusions:: Stereo-EEG, with the substantial contribution of intracerebral stimulations, allows to localize/lateralize language areas and to accurately define the boundaries and reciprocal relationship with the epileptogenic zone and the anatomical lesion.
KNOWLEDGE OF WOMEN ISSUES AND EPILEPSY AMONG DOCTORS IN SUDAN

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Background and Aims:: The objective of this study was to assess the knowledge of doctors in Sudan about women issues related to epilepsy.

Methods:: In this cross-sectional study that was conducted in Sudan during the period from October to December 2017, we used Google forms to collect data from 154 doctors using Knowledge of Women Issues and Epilepsy (KOWIE) II standardized questionnaire.

Results:: Our studied group included house officers (n = 34), medical officers (n = 60), registrars (n = 52), and specialists (n = 8). The majority of participants were aware of the role of folic acid in reducing teratogenicity of antiepileptic drugs (AEDs) (89%) and that women with epilepsy (WWE) should continue taking their AEDs during pregnancy (76.6%). Two-thirds of participants knew that most WWE have healthy children (68.2%) and that enzyme-inducing AEDs may reduce effectiveness of some contraceptives (72.1%). Half of participants were aware of the association between AEDs and osteomalacia (50%), and more than one-third (38.3%) knew that women taking AEDs can safely breastfeed (38.3%). Only (20.1%) knew that WWE have a higher incidence of sexual dysfunction compared with women without epilepsy, and only some (15.6%) knew that estrogen has a proconvulsant effect while progesterone has anticonvulsant qualities. The mean score of our participants was 5.53 out of 10 (standard deviation (SD) ± 1.64).

Conclusions:: In this small cross-sectional study, Sudanese doctors' knowledge was not satisfactory regarding the majority of questions on KOWIE II. Further education and training are indicated to decrease this knowledge gap and to improve care of WWE.
Background and Aims:: Perampanel is a once-daily oral anti-seizure medication (ASM) for focal-onset seizures (FOS) and generalized tonic-clonic seizures. The AMPA Study (501; NCT04257604) was a multicenter, prospective, observational study conducted in Italy to assess the effectiveness and safety of perampanel received as add-on therapy in patients aged ≥12 years with FOS in a real-world setting. We present the design of the AMPA Study.

Methods:: Inclusion criteria included: aged ≥12 years; diagnosis of FOS with or without focal to bilateral tonic-clonic seizures (FBTCS); prescribed perampanel according to the Summary of Product Characteristics (decision to initiate perampanel had to be independent of study participation); seizures inadequately controlled with 1–3 ASMs; available seizure-frequency data at baseline. Exclusion criteria included: any contraindication to perampanel use; pregnant/lactating women; clinically significant psychiatric illness or psychological/behavioral problems; moderate-to-severe renal impairment; severe hepatic impairment. Patients were assessed at baseline, and following 3 (visit 1), 6 (visit 2), and 12 months (final visit) of perampanel treatment. The primary endpoint was median percentage change from baseline in the frequency of all seizures at 6 months. Secondary endpoints included: retention rates; responder and seizure-freedom rates; median percent change in FBTCS frequency; adverse drug reactions; the Quality of Life in Epilepsy Questionnaire and Epworth Sleepiness Scale scores (adults).

Results:: Overall, 243 patients have been enrolled at 19 sites across Italy.

Conclusions:: The AMPA Study will provide important prospective, observational, real-world data on the use of perampanel as an add-on treatment in patients aged ≥12 years with FOS. Funding: Eisai s.r.l.
ORAL HEALTH STATUS OF PATIENTS WITH EPILEPSY IN RURAL POPULATION

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**Background and Aims:** The present study was undertaken for assessing the oral health status of patients with epilepsy in rural population of Himachal.

**Methods:** A total of 100 epilepsy patients were enrolled in the present study. Complete demographic details of all the patients were obtained. A Performa was prepared and separate assessment of clinical and medical details of all the patients was done. After obtaining the informed consent, patients were made to sit in supine position and complete oral examination was carried using mouth mirror, William probe and explorer. OHI-S (Oral hygiene index- simplified) was used for assessing the oral health status. All the results were recorded in Microsoft excel sheet and were analysed by SPSS software.

**Results:** It was seen that significantly higher proportion of patients with history of seizure of more than 4 didn’t brushed their teeth regularly. Incidence of bleeding gums was significantly higher among patients history of seizure of more than 4 per month in comparison to patients which were seizure free. Out of 14 patients with history of seizure of more than 4 per month, bad breath was present in 12 patients while out of 20 patients which were seizure free, 6 patients had bad breath. While analysing statistically, it was seen that bad breath was strongly associated with frequency of seizures. Also, significantly higher proportion of dental caries and gingivitis was seen in patients with higher frequency of seizure per month.

**Conclusions:** Conclusion: Epilepsy patients have compromised oral health and hence; regular oral examination is advocated in these group of patients.
Background and Aims:: In the first year of life, epilepsy causes a serious neurological problem. Severe sequelae are possible in the preterm child with the cerebral immaturity. This study aims to establish the relationship between premature birth and the epilepsy through our two populations study.

Methods:: This is a retrospective case-control study conducted at the Antsakaviro Neuroscience and Mental Health Laboratory from January 2015 to January 2017. We selected as cases all children aged 0 to 12 months old with epilepsy and compared them with control children aged 0 to 12 months without epilepsy in the laboratory of neurosciences and mental health.

Results:: We have 530 epileptic patients aged 0-12 months and 530 children aged 0-12 months without epilepsy as controls. The average age was 5.52 months and the sex ratio was 1.5. Twenty-two percent were premature (n = 97) and 81% not premature (n = 433). Among non-epileptics 5.84% (n = 31) were premature. Being premature would increase the occurrence of epilepsy 4 times more (OR: 3.6).

Conclusions:: Prematurity is a risk factor for epilepsy in the first year of life. A neurological oversight of premature is necessary to detect the epilepsy.
ELECTROCLINICAL ASPECTS OF OCCIPITAL EPILEPSY SEEN IN THE NEUROSCIENCES AND MENTAL HEALTH LABORATORY ANTSAKAVIRO

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¹CHU Antanambao, Medicine, toliara, Madagascar, ²Faculty of Medicine of Antananarivo, Neurology, Antananarivo, Madagascar

Background and Aims:: Occipital epilepsy occurs when the initial site of epileptic discharge involves part or all of the occipital lobe. Occipital epilepsy is the least common of the other types of epilepsy and is rarely described in the literature. However, the manifestation located initially in the occipital cortex, which is a functional zone of vision, leads to its protean aspect. It can be a source of diagnostic wandering. The purpose of this study is to describe the electroencephalographic clinical characteristics of patients seen for occipital epilepsy at the Laboratory of Neurosciences and Mental Health, Antsakavigro, Madagascar

Methods:: This is a retrospective and descriptive study that took place over a one-year period (January 2016 to December 2016). Included in this study were all patients diagnosed with clinically and EEG-confirmed occipital epilepsy. A correlation between clinical manifestations and electroclinical data is sought.

Results:: We retained 66 patients with male predominance (sex ratio: 1.4). The age of the patients ranged from 3 to 55 years with a mean age of 13.77 years. Patients reside in urban areas and the majority are of non-school age. The clinical manifestations of occipital epilepsy are mainly paroxysmal visual hallucinations lasting on average 3 minutes and of variable frequency. EEG signs are predominantly paroxysmal activities with a predominant or occipital starting point.

Conclusions:: The clinical and electroencephalographic manifestations of occipital epilepsy deserve special attention in order to make a proper diagnosis.
Background and Aims:: Tuberous sclerosis complex (TSC) or Bourneville’s disease, first described by Desiree- Magloire Bourneville in 1880, is a rare genetic disorder of autosomal dominant inheritance with the prevalence of one in 6000 live birth, affecting both sexes and all ethnic groups1,2. It is a multisystem disorder involving brain, skin, kidneys, heart, eyes, and lungs which becomes apparent only in late childhood, limiting the usefulness for early diagnosis in infancy. Tuberous sclerosis is a rare neurocutaneous syndrome and the major neurological manifestations are seizures, autism, developmental delay and behavioral and psychiatric disorder. Epilepsy is the most common nervous system performance in children tuberous sclerosis complex (TSC), and the main types of onset are partial seizures and spasms.

Methods:: 7 year old boy referred from paediatric op with complains of involuntary movements of right upper limb with up rolling of eye ball and loc for 5min. he had similar episodes in the day before. no history of any fever. on examination conscious, oriented, head to toe examination revealed Doliophealy, adenoma sebaceum, ash leaf Macules in over back, thigh

Results:: Routine blood investigation are normal, mri imaging suggestive of tuberous sclerosis, dermatologist opinion also confirmed the same

Conclusions:: TSC is one of the neurocutaneous syndromes inherited in autosomal dominant fashion with almost complete penetrance with variable expressivity, affecting almost all organs. The quality of life depends on the neurological manifestation like seizures and mental retardation which is improved by multidisciplinary approach and symptomatic organ specific treatment. Clinical diagnosis complementing with DNA testing allows precise genetic counseling, which is important.
SLEEP DISORDERS IN CHILDHOOD EPILEPSY

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Background and Aims:: sleep has a great influence on epileptic seizures and epilepsy significantly affects the quality and restorative functions of sleep. Clinical research has found a fairly high prevalence in children with epilepsy compared to healthy children .The aims of our study: -Study the risk factors for sleep disorders in children with epilepsy -Identify the most frequent sleep disorders

Methods:: This is a case-control study, carried in the neurology department of Tlemcen University Hospital. The questionnaire on children's sleep habits (CSHQ) was used. A total score of 41 is a sensitive threshold for clinically significant sleep problems. The Children's Quality of Life Questionnaire (KINDL-R) . Factors related to epilepsy were evaluated, in addition to questioning with parent. Patient informations were collected such as age at diagnosis, type of epileptic seizures, duration of epilepsy, and treatment. Statistical study was carried SPSS(22).

Results:: 59 children and adolescents with epilepsy and 28 controls were included in the study. The mean age of the epilepsy and control groups was 12.2 ± 2.45 and 1.8 ± 1.25, respectively. In the epilepsy group, 54.2% presented with generalized epilepsy, 32.2% with partial epilepsy. The majority of patients had seizures once a year (79.6%). 76.2% of patients were on antiepileptics monotherapy. Comparison of CSHQ scores between children with epilepsy and controls concluded that the total score and CSHQ subscores were higher in the epilepsy group (p <0.005). The KINDL-R total score was lower in children with epilepsy.

Conclusions:: Sleep disorders in epilepsy childhood not only predispose to mood, cognitive and behavioral disturbances, but also have a significant impact on physical health.
PREDICTORS OF ACUTE SYMPTOMATIC SEIZURE IN PATIENTS WITH CENTRAL NERVOUS SYSTEM INFECTIONS IN THE NEUROLOGY DEPARTMENT OF MOEHAMMAD HOESIN PALEMBANG HOSPITAL PALEMBANG INDONESIA

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Background and Aims:: Acute symptomatic seizure (ASS) is defined as a clinical seizure occurring in acute temporal relationship close to the central nervous system (CNS) which may be due to metabolic, toxic, structural lesions, infection or inflammation. Seizures and coma are known predictors of poor outcome in patients with CNS infection. This study aims to identify various factors that can be predictors of ASS incidence in patients with CNS infection.

Methods:: This is a cross sectional analytic observational study at Mohammad Hoesin Hospital Palembang from January 1, 2019 to December 31, 2020. The populations were all CNS infections inpatients. Sampling was carried out through medical record data.

Results:: A total of 56 CNS infection patients were included as samples and 27 people had ASS. ASS was more common in the 18-30 years age group, female, with clinical fever, with > 4 neurological manifestations, with history of HIV, normal leukocytes, hyponatremia, hypocalcemia and GCS <12. Patients with GCS <12 who experienced ASS had a poor prognosis, as evidenced by 71.43% of them died. The majority of the etiology is cerebral toxoplasmosis and the most common head CT scan is cerebral edema. After analyzing bivariate and multivariate statistically, there was not even one variable that had a significant result as a predictor of ASS in patients with CNS infection (P>0.05).

Conclusions:: In this study, the proportion of independent variables studied as predictors of ASS in CNS infection patients was quite significant according to theory, literature and previous studies, although not statistically significant.
Background and Aims:: DNETs are the primary tumor etiology of drug-resistant temporal epilepsies in children and young adults. It is a benign neuroglial and neuronal or mixed tumor, with a cortical site, involving 23.4% of all tumors associated with epilepsy. We illustrate through 3 cases the clinical and radio-diagnostic characteristics of DNETs as well as their different therapeutic and evolutionary modalities.

Methods:: We report the cases of 3 patients followed in our department for DNET
We note the recurrence of EMEs for the 1st patient with neuropsychiatric disorder, occasional epileptic seizures for the 2nd patient, paroxysmal headache for the 3rd patient.
Conclusions: Status epilepticus or early-onset drug-resistant complex partial seizures are the classic inaugural pictures of DNETs. Late onset after the age of 20 and immediately generalized seizures are rare. These tumors can be asymptomatic. Radiologically, these tumors have cortical site, often temporal in 60%, or frontal in 30% rarely. Surgical excision is the basic treatment.

<table>
<thead>
<tr>
<th>case/sexe</th>
<th>Age of epilepsy onset</th>
<th>seizure type</th>
<th>lesion location</th>
<th>MRI characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>case1, male 57 years</td>
<td>6 years</td>
<td>onset of focal right clonic then secondary generalization (tonicoclonic)</td>
<td>Slowly evolving left frontal cortex</td>
<td>heterogeneous lesion site of calcification and a fluid component</td>
</tr>
<tr>
<td>case2, male 60 years</td>
<td>24 years</td>
<td>onset of left focal point (eye and mouth deviation) then secondary generalization (tonicoclonic and revulsion of the eyeballs)</td>
<td>Left internal temporal cortex.</td>
<td>pseudocystic lesion</td>
</tr>
<tr>
<td>case3, female 43 ans</td>
<td>6 years</td>
<td>from the outset generalized Tonicoclonic</td>
<td>Left parietal cortex</td>
<td>cortical lesion making an impression on the cranial vault</td>
</tr>
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</table>
PROGRESSION OF NEURONAL DAMAGE IN MESIAL TEMPORAL LOBE EPILEPSY MEASURED BY PROTON MAGNETIC RESONANCE SPECTROSCOPY

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Background and Aims:: Mesial temporal lobe epilepsy (MTLE) presents with pharmacoresistance. Progression of structural damage has been reported, but it is unclear whether there is progression of metabolic damage. We aimed to longitudinally investigate metabolic changes in patients with MTLE with and without pharmacoresistance, using proton magnetic resonance spectroscopy (1H-MRS), to quantify N-acetylaspartate (NAA), a marker of neuronal damage and dysfunction.

Methods:: We measured ipsi- and contralateral hippocampal NAA ratios to creatine (NAA/Cr) using 1H-MRS from 167 individuals: 66 pharmacoresponsive patients, 95 pharmacoresistant patients and 6 controls. We selected up to four 1H-MRS per patient. We performed generalized linear models with identity link function. The main effects were pharmacoresponse, time, and pharmacoresponse*time interaction. We covaried for age at each scan. We set p<0.05 as significant.

Results:: There were effects of time (p=0.039), and pharmacoresponse (p=0.024) but no pharmacoresponse*time (p=0.082) interaction on ipsilateral NAA/Cr. We found reduced ipsilateral NAA/Cr in pharmacoresistant patients compared to pharmacoresponsive patients (p=0.043) and controls (p=0.004). Both pharmacoresponse groups showed reduced NAA/Cr comparing scan-1 to scan-3 (p=0.006) and scan-4 (p=0.051); and comparing scan-2 to scan-3 (p<0.001) and scan-4 (p=0.012). We found no effect of pharmacoresponse nor interactions on contralateral NAA/Cr (p>0.12) and only effect of time (p=0.037) on contralateral NAA/Cr (p=0.037). There was reduced contralateral NAA/Cr comparing scan-1 to scan-2 (p=0.034), regardless pharmacoresponse.

Conclusions:: Our data suggest unilateral effects of pharmacoresponse and bilateral effects of time in neuronal damage. Acknowledgements: This study was funded with grants Pibic-CNPQ (129161/2020-9) and Fapesp (2013/07559-3)
EARLY AND LATE SEIZURES IN MALIGNANT MIDDLE CEREBRAL ARTERY STROKE TREATED WITH DECOMPRESSIVE CRANIECTOMY AND: PRELIMINARY RESULTS OF A SINGLE CENTER REGISTRY.

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Background and Aims:: More than 40% of patients with malignant middle cerebral artery (MCA) stroke undergone craniectomy may develop both early or late seizures, mainly partial with generalization. The median onset of seizures was seven months; delayed craniectomy (>42h) has been identified as a risk factor for seizure (1, 2). The aim of our study was to identify factors related to the occurrence of seizures.

Methods:: All patients who developed malignant MCA infarction and undergone decompressive craniectomy in Modena Stroke Unit between september 2008 and june 2021 were evaluated. Clinical features -including mRS at 3 and 12 month follow up- and neuroradiological parameters were collected.

Results:: We evaluated a total of 61 patients. Seizures occurred in 42,6 % of all patients (26/61 pt). The median time from stroke onset to craniectomy was 47,1 hours all patients, but was 72 h in epyleptic. The median onset of seizures was 162 days but in 8/26 pt they started within 20d from stroke onset. The majority of these were focal motor seizures with generalization. Large craniectomy were slightly related with early seizures. At 1 year follow up 3/26 pt were died (mRS=6) and 20/26 presented good functional outcome (mRS<=4). Two of them needed a second cranioplasty intervention because of a major seizure.

Conclusions:: Epileptic seizures in patients with malignant MCA infarcts submitted to DHC is very frequent and can occur early or lately, affecting the clinical outcome.
VIOLENCE AND EPILEPSY: DESCRIPTIVE STUDY OF 33 CASES

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Background and Aims:: Questions are often raised about the relationship between recurrent seizures and the behaviour of the epileptic person. However, some people who have seizures have behavioural problems and are responsible for medico-legal procedures despite the progress of anticomitial chemotherapy. The objective of this work is to develop the sociodemographic and clinical profile found in epileptic patients who committed violent acts.

Methods:: This is a retrospective study of epileptic patients hospitalized at the psychiatry department in the university hospital of Mahdia.

Results:: A total of 33 files were collected, 75% of patients were admitted according to the mode of involuntary hospitalization. The most frequent reason for hospitalization was motor instability (80% of cases). The average age was 31.8 years old, sex ratio was 2.2. The level of education was low in 93% of cases, the majority (90%) of cases was without professions, single in 81% of cases. The criminal record was found in 21% of cases whereas the psychiatric history in 37% of cases: depressive disorder represents the first comorbidity found 25% of cases, psychotic disorders in 12% of cases and bipolar disorder in 6% of cases. Mental retardation and personality disorders associated with epilepsy are objectified in 62% and 12% of cases respectively. These patients were all treated with antiepileptics, 56% with thymoregulators, 37% with antipsychotics, 25% with antidepressants and 18% with benzodiazepines.

Conclusions:: It is important to recognize a psychiatric disorder related to epileptic seizure to adopt the therapeutic measures and to prevent the passage to the violent act.
THE WHITE ROSE PETAL EXTRACT ABROGATES EXCITOTOXIC NEURONAL DAMAGE THROUGH ANTIOXIDATIVE AND ANTI-INFLAMMATORY ACTIVITIES

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Background and Aims:: Since oxidative stress and inflammation are involved in seizure-related neurotoxicity, the neuroprotective effect of a white rose (Rosa hybrida) petal extract (WRPE) in mice that are challenged with kainic acid (KA) were examined using behavioral epileptiform seizures as well as biochemical and morphological parameters of oxidative stress and inflammation.

Methods:: WRPE was orally administered to ICR mice for 15 days, and intraperitoneally challenged with KA. Seizure activity, lipid peroxidation, inflammatory cytokines, and related enzymes were analyzed in the brain tissue, and the morphological alterations in the hippocampal pyramidal neurons. Antioxidant ingredients in WRPE were analyzed, and antioxidant, anti-inflammatory, and neuroprotective activities of WRPE were investigated in human neural stem cells.

Results:: Total polyphenol and flavonoid contents in WRPE were 303.3 ± 15.3 mg gallic acid equivalent/g extract and 18.5 ± 2.2 mg catechin/g extract, respectively. WRPE exhibited strong radical-scavenging activities and inhibited lipid peroxidation in vitro, and protected glutamate-induced cytotoxicity in NSCs by suppressing inflammatory process. Treatment with WRPE attenuated epileptiform seizure scores in KA-challenged mice, and decreased hippocampal pyramidal neuronal injury and loss as well as astrocyte activation. Lipid peroxidation was inhibited, and mRNA expression of antioxidant enzymes (GPx, PHGPx, SOD1, and SOD2) were recovered in the brain tissues. Inflammatory parameters including NF-kB, IL-1, TNF-α, IL-6, HMGB1, TGF-β, iNOS, COX2, and GFAP mRNAs and proteins were also down-regulated by WRPE treatment.

Conclusions:: Taken together, the results indicate that WRPE could attenuate KA-induced brain injury through antioxidative and anti-inflammatory activities, and that WRPE and their active ingredients could be candidates for neuroprotective drugs and functional foods.
MENTAL HEALTH AND EPILEPSY: A SURVEY EXPLORING PERSPECTIVES OF HEALTHCARE PROVIDERS IN SUB-SAHARAN AFRICA

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¹Queen's University Belfast, School Of Medicine, Dentistry And Biomedical Sciences, Belfast, United Kingdom, ²Pretola Global Health Consulting Limited, Ilae Uk, Isle of Wight, United Kingdom, ³University of Plymouth, Peninsula School Of Medicine, Plymouth, United Kingdom

Background and Aims:: Epilepsy is the most common neurological diagnosis reported in sub-Saharan Africa, and psychological distress, particularly depression, is highly comorbid. Yet most patients fail to receive appropriate multidisciplinary care. This study addressed attitudes towards epilepsy and comorbid mental illness, as well as management practices among healthcare providers in sub-Saharan Africa. Additionally, we explored the perceived local barriers to adequate psychiatric care.

Methods:: A cross-sectional survey was conducted, and distributed using a snow-balling method, among healthcare providers in sub-Saharan African settings who were attending virtual training from Pretola Global Health and Consulting Ltd.

Results:: Our survey received responses from 203 healthcare professionals in sub-Saharan African countries. Most (80.0%) recognised a positive association between mental illness and epilepsy. However, only a small proportion reported that they screen for (14.4%) or provide education on the risk of developing mental illness (12.4%) in epilepsy populations. The vast majority (93.5%) reported that treatment improvements within their local healthcare settings are required. The major themes identified as local barriers to adequate psychiatric care were a lack of confidence in how to assess for mental illness; lack of awareness that there is a heightened risk of mental illness in patients with epilepsy; and limited access to psychological services.

Conclusions:: Our study highlights the need for improving access to quality treatment of mental health disorders in epilepsy populations in sub-Saharan Africa. Our practical recommendation is to provide accessible training to sub-Saharan African healthcare providers by way of a validated, online education programme detailing optimal multidisciplinary care of mental illness in epilepsy populations.
HYSTERO-EPILEPSY, DIAGNOSTIC AND THERAPEUTIC DIFFICULTIES

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2University Hospital of Mahdia, Psychiatry, Mahdia, Tunisia,
3Department of Neurology, Mahdia, Taher Sfar University Hospital, Tunisia,
4University Hospital of Mahdia, Psychiatry, Mahdia, Tunisia

Background and Aims:: The problem of the differentiation between epileptic seizures and hysterical attacks recurs constantly in the history of medicine. Hysteroepilepsy or non-epileptic psychogenic seizures (NEPC) can be defined as paroxysmal manifestations clinically evoking epileptic seizures but related to unconscious psychogenic processes. The clinical diagnosis is particularly difficult. The objective of this work is to determine the epidemiological and evolutionary characteristics.

Methods:: This is a retrospective study of the files of patients hospitalized in the department of Medicine who have been diagnosed with hystero-epilepsy.

Results:: We collected 32 patients. The average age was 26 years. The sex ratio was 0.61. The reason for hospitalization was the recrudescence of pharmaco-resistant paroxysmal manifestations. Three had a history of epilepsy, the others were free of all organic and psychiatric pathologies. The crises described were of tonicoclonic type in 6 cases. The clinical symptomatology is insufficient to carry the diagnosis requiring the use of biological and radiological explorations (cerebral computed tomography performed in 14 patients returned normal). Video-ectroencephalographic (EEG) done in all patients were without abnormalities. The treatment initiated was intravenous benzodiazepines in 21 patients. The evolution was marked by the recurrence of the symptomatology for 25% of the cases for which they were hospitalized.

Conclusions:: Hysteroepilepsy is a significant cost to the health care system. Early diagnosis avoids anticonvulsant therapy, which is ineffective and has frequent side effects.
MOTOR AND COGNITIVE DYSFUNCTIONS IN RELAPSING-REMITTING MULTIPLE SCLEROSIS: THE ROLE OF STRUCTURAL BRAIN DAMAGE

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Background and Aims:: A deeper understanding of the relationship between motor and cognitive dysfunctions in multiple sclerosis (MS) could highlight overlapping mechanisms of impairment. We assessed the influence of brain structural damage and cognition on motor performance in a large group of MS patients.

Methods:: Eighty-six healthy controls (HC) and 127 relapsing-remitting (RR) MS patients underwent 3.0T MRI, the Brief Repeatable Battery of Neuropsychological tests and a functional examination including finger tapping test (FTT), nine-hole peg test (9-HPT), 25-foot walk test (25-FWT) and expanded disability status scale (EDSS). Clinical outcomes were converted to z-scores and analyzed according to the side of greatest upper-limb impairment. Univariate analyses and hierarchical linear regression were computed to investigate the association between demographic and clinical features, cognitive scores, MRI measures, and functional outcomes.

Results:: In RRMS patients, spatial recall test correlated with FTT performed with the preserved side (PS), bilateral 9-HPT and T25FW (p≤0.033); Symbol Digit Modalities Test was associated with FTT performed with the impaired side (IS) and bilateral 9-HPT (p≤0.022); while Word List Generation (WLG) correlated with PS-FTT and bilateral 9-HPT (p≤0.045). After adjusting for the side of impairment, hierarchical regression models selected clinical and demographic features as predictors of bilateral FTT (R²=0.15-0.23), while EDSS and normalized brain volume (NBV) were significant for T25FW (R²=0.21) and for IS-9-HPT (with the additional contribution of T1 lesion volume, R²=0.32). EDSS, sex, NDGMV and WLG predicted variability in PS-9-HPT (R²=0.31).

Conclusions:: In RRMS patients, motor and cognitive dysfunctions are related, and their association is mediated by structural brain damage.
WORSENED VISUAL HALLUCINATION IN DEMENTIA LEWY BODY RELATED TO SYMPTOMATIC THERAPY

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Background and Aims:: Lewy Body Dementia (DLB) is consists of fluctuating cognition, recurrent visual hallucinations, REM sleep behaviour disorder, and cardinal features of Parkinsonism. This case report purposes of describing progressivity of visual hallucination in DLB who get symptomatic therapy.

Methods:: A case report: a woman, 84 years old, with progressive cognitive dysfunction (orientation, attention, calculation) since two years ago then worsened in 6 months and affected her daily living activities, so the patient received symptomatic treatment for dementia (donepezil 5 mg) since these last 6 months. She has a history of visual hallucinations for more than ten years, which has improved in the past year but worsens in these three months. On the other side, she was diagnosed with Parkinson's Disease 3.5 years ago and got therapy: Levodopa/Benserazide for 3.5 years.

Results:: This case illustrates worsening visual hallucinations by increasing frequency and form of visual hallucinations in DLB related to symptomatic therapy (dopaminergic/levodopa). Levodopa is related to intrinsic striatal pathology, reduced caudal putamen dopamine D2 receptors, and D3 receptors on corticostriatal projection neurons, with the strongest association in anterior cingulate, develop visual hallucinations.

Conclusions:: DLB is a progressive disease that could be getting worse in the patients. We have to select DLB patients' treatments as substantial since the treatment of non-motor and motor symptoms might be interacting with one another. Hence, it aggravates clinical manifestation in DLB. Non-pharmacological strategies should be conducted as soon as possible to prevent worsening conditions.
Background and Aims:: Raising a child with developmental delay is a profoundly difficult experience for parents of these children. This study was aimed to compare the stress level and life participation among mothers of children with Down Syndrome (DS) and Cerebral Palsy (CP). And to identify whether the stress and life participation of the mothers differ significantly based on the functional skills of children. Methods:: A total of 78 parents (of children with CP, n = 42; of children with DS, n = 34) were examined using Pediatric Evaluation of Disability Inventory (PEDI) and Perceived Stress Scale (PSS) and Life Participation for Parents (LPP). Results:: It was found that mothers of children with CP had significantly higher perceived stress scale scores and had significantly lower life participation scores than mothers of children with DS (p=0.010; p=0.046, respectively). It was found that children with CP had lower functional level (FL) scores than children with DS (p=0.011). The children’s FL may have been related to the stress level and life participation of their mothers. Conclusions:: Findings indicated a significant difference between mothers’ stress levels and life participation according to the functionality level of the children. These findings highlight the need for family support services for these mothers. Further studies may also compare the stress level and life participation of fathers who had children with a disability.
STUDY OF SELF CONCEPT AND SOCIAL SUPPORT PERCEPTION: NEURODEVELOPMENTAL DISORDERS

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Background and Aims:: This study were planned to investigate self-perception, self-esteem, and social support perception among children with Attention Deficit and Hyperactivity Disorder (ADHD) and/or Specific Learning Disabilities (SLD).

Methods:: In this study, 31 children with ADHD and/or SLD between the ages of 9-13 who are registered in Hacettepe University Faculty of Health Sciences, Department of Occupational Therapy were included as a research group (RG). Thirty typically developed children between the same age (9-13 years old) were included as the control group (CG). For this study, Self-Perception Profile for Children (SPPC), Coopersmith Self-Esteem Inventory (CSEI), and Social Support Questionnaire for Children (SSQC) were used. Mann-Whitney U test was used for analysis.

Results:: The analyses showed that the SPPC score of the RG was significantly lower than that for CG (Z=-3.125; p=0.002); the CSEI score of the RG was significantly lower than that for CG (Z=-2.464; p=0.014) and the SSQC score of the RG was significantly lower than that for CG (Z=-2.887; p=0.004).

Conclusions:: In this study, it was found that self-concept, self-esteem, and social support are low from the typical developed peers. Children with ADHD with/or SLD have problems these psychosocial areas and need support. Therefore, it is important to include practices that support their identity development and social support in their rehabilitation programs.
Background and Aims:: The sporadic nature AD suggest that aside from biological determinants, environmental factors such as stress plays a role in the development of disease. This study aims to analyze the relationship between stressful life events and AD.

Methods:: We studied 118 patients with diagnosis of AD. Medium age was 73 years. Meantime elapsed from the initial symptoms was 2.6 years. A control group of 81 healthy individuals was studied. A questionnaire looking for stressful life events in the 3 years before diagnosis of AD was performed to patients, caregivers and controls.

Results:: In the AD group, 85 patients (72%) presented a history of significant stressful life events, 2.1 years (SD 1.4 y) before the onset of symptoms. The most common findings in the AD group were: couple death (24 cases), child death (15 cases), history of assault (21 cases), history of car accident (11 cases). Other stressful situations were marked financial problems, bereavement, retirement, adaptive changes due to migrations and diagnosis of severe somatic disease in the family. In the control group, only 21 individuals (26%) recognized similar previous stress factors.

Conclusions:: We observed an association between stressful life events preceding the onset of dementia in a high percentage of our patients. Stress could trigger the degenerative process in AD and growing evidences suggest a dysfunction in neuroendocrine and immune system. According our results, we can establish a relationship between several stressful life events and the onset of dementia. It is an observational finding and does not imply direct causality.
SPEECH-LANGUAGE PROFILES IN EARLY-STAGE PRIMARY PROGRESSIVE APHASIA: NON-FLUENT VERSUS SEMANTIC VARIANT

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Background and Aims:: Primary progressive aphasia (PPA), a clinical syndrome caused by neurodegenerative pathology, is subdivided into three variants depending on the profiles of language impairment: non-fluent, semantic, and logopenic variant (nfvPPA, svPPA, lvPPA). This study compared the language characteristics of the patients in their early stage of PPA.

Methods:: Fifty-five patients were referred to our speech-language clinic from 2007 to 2019 to rule out PPA. Among them, 34 patients demonstrate mild language impairment (more than 80 of AQ score in K-WAB). Finally, 5 nfvPPA and 3 svPPA cases were included after the review of neuroimaging and follow-up studies for analysis. The results of a language battery (K-WAB), naming deep-tests (K-BNT and COWAT) and acoustic analysis of spontaneous speech were compared.

Results:: The patients in both groups presented mild anomic profile of aphasia and had no significant differences in each subtest (fluency, informativeness, auditory comprehension, repetition, and naming) as well as AQ score in K-WAB. However, in naming deep-tests, the nfvPPA was significantly impaired in phonemic generative naming, whereas the svPPA presented significant decline in confrontation naming and semantic generative naming. Acoustically, the nfvPPA produced shorter length of utterances, prolonged pause, and slower speech rate during their spontaneous speech compared to the svPPA.

Conclusions:: The results of this study demonstrated different speech-language characteristics between two subtypes of PPA even in their early stage, which were not distinguished by a standardized language battery. It may provide clinically useful information for early differential diagnosis of PPA subtypes. Further researches including all three variants with larger participants group are needed.
CONSUMPTION OF PROCESSED MEAT MAY INCREASE THE RISK OF INCIDENT LATE-ONSET DEPRESSION

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Background and Aims:: The possible relationship between dietary habits and the incidence of late-onset depression (LOD), defined as first onset depression in mild-life (between 45 and 65 years), is unclear. The present study was aimed at investigating the relationship between consumption of different foods and incident LOD.

Methods:: In a longitudinal population-based study with a 12-year follow-up, 546 community-dwelling subjects in Southern Italy aged ≥ 65 years (mean age = 66 years) were recruited. Dietary intake was assessed with a food frequency questionnaire. Depressive disorders, classified on the basis of the age of onset at follow-up, were assessed by means of the Semi-structured Clinical Diagnostic Interview for DSM-IV-TR Axis I Disorders.

Results:: At baseline, subjects with incident LOD had lower scores on a test assessing global cognition (Mini-Mental State Examination), lower total cholesterol levels, and higher body mass index. Only processed meat (with high content of salt, saturated fats and preservatives) significantly increased the risk of incident LOD of about 10% by 5 g/day intake (fully-adjusted model, hazard ratio:1.13, 95% confidence interval:1.04-1.22). The average consumption of processed meat was 21 g/d in subjects with incident LOD and 15 g/d in individuals without incident LOD. A similar risk relation was found for intake of single foods forming processed meat group (sausages, salami, and mortadella, baked ham), but not for raw ham.

Conclusions:: These findings suggest that in midlife a higher intake of processed meat might not only increase the risk of cardiovascular- and metabolic-related chronic diseases, but also increase the risk of LOD.
EXAMINATION OF THE RELATIONSHIP BETWEEN PARENTAL BEHAVIORS AND EXECUTIVE FUNCTIONS-SOCIAL SKILLS OF TYPICALLY DEVELOPED CHILDREN

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Background and Aims:: Children's developmental, social and cognitive skills are of great importance. It is thought that various skills are associated with parental behaviors in childhood. This study was aimed to investigate the relationship between parental behavior and children's executive functions and social development.

Methods:: Assessments were conducted with 103 parents with typically developing children between the ages of 7-12. Sociodemographic Information Form, the Social Skills Assessment Scale, the Childhood Executive Function Inventory, and the Parental Behavior Scale were administered to parents. Correlation analysis (Pearson Correlation coefficient) was a statistical method used to evaluate the strength of the relationship between these three variables.

Results:: There was a relationship between the score of the Childhood Executive Function Inventory and the score of the Social Skills Assessment Scale (r = 0.472; p < 0.001); the Parental Behavior Scale (r = 0.300; p = 0.002). In addition, there was no relationship between the score of the Social Skills Assessment Scale and the Parental Behavior Scale (r = -0.048; p = 0.629).

Conclusions:: According to the findings, only executive functions were found to be associated with parental behavior. Although these executive functions and social skills are related, social skills are not related to parental attitudes. Therefore, it is thought that parents' attitudes can be positively affected when executive functions are developed with training.
MENTAL DEPRESSION AND ASSOCIATED FACTORS AMONG ADULTS CONSULTING AT THE BAMENDA REGIONAL HOSPITAL, CAMEROON

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Background and Aims:: Depression is a common mental disorder, characterised by low mood that lasts for long and affects everyday life. It has serious consequences on quality and length of life but is still frequently misdiagnosed and underdiagnosed in low- and middle-income countries. This study was designed to estimate the burden of depression among adults consulting at Bamenda Regional Hospital, in the North-West Region of Cameroon.

Methods:: This was a cross-sectional study carried out over a period of 4 months, in the Bamenda Regional Hospital. Adults consulting at the Outpatient Department were included in the study and screened for depression using the PHQ-9 questionnaire. People with past diagnosis of mental illness, presenting primarily for a psychiatric consultation, and cognitively impaired subjects were excluded. Data were entered and analysed using SPSS version 25 for Windows.

Results:: A total number of 151 people were screened for depression. The prevalence of depression was 47%. Female gender and smoking were significantly associated with depression. Suicidal thought (and even attempt) was observed in 0.7% of participants, while suicidal ideation (1 in 6 participants) and self-harm (6%) were common in this population.

Conclusions:: There is high prevalence of depression in the general outpatient population in the Bamenda Regional Hospital. Therefore, it is important to ensure efficient depression screening at the outpatient department, especially for female patients and smokers. Physicians should be aware of this burden.
DEPRESSION AND ANXIETY AMONG STUDENTS OF THE FACULTY OF HEALTH SCIENCES OF THE UNIVERSITY OF BAMENDA, CAMEROON

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Background and Aims:: Mental health among university students represents an important and growing public health concern for which epidemiological data are needed. The main aim of this study was to estimate the magnitude of anxiety and depression among the students of the Faculty of Health Sciences of the University of Bamenda.

Methods:: This was a cross-sectional study among students of Faculty of Health Sciences of the University of Bamenda. The participants were screened for depression and anxiety using the 9-Item Patient Health Questionnaire (PHQ-9) and the 10-item Kessler Psychological Distress Scale questionnaire (K10) respectively. The questionnaires were self-administered through an online survey targeting students of the Faculty of Health Sciences. Data was analysed using Statistical Package for Social Sciences SPSS software.

Results:: About 17.4% of participants had major depressive disorder (PHQ-9 Score ≥ 10) while 15% had psychologically distress (K10 Score ≥ 25). Major life-changing crisis, regrets studying medicine, enrolment in medical laboratory sciences or nursing studies, low self-reported GPA, and resit examination were all significantly associated with depression. Major life-changing crisis, regret studying medicine, medical laboratory sciences or nursing were significantly associated with anxiety. There was no association between anxiety and self-reported academic performance (GPA), OR: 0.63(0.32-1.24) and p-value=0.182.

Conclusions:: Depression and anxiety are common among students of the Faculty of Health Sciences of the University of Bamenda. Major life-changing events, having regrets of studying Medicine, enrolment in medical laboratory sciences or nursing studies, and poor academic performance were associated with depression.
PREVALENCE OF DEPRESSION AMONGST STROKE SURVIVORS IN TWO REGIONAL HOSPITALS IN CAMEROON

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Background and Aims:: Stroke has numerous complications, with a major being post-stroke depression (PSD). This condition, which has significant impact on functional recovery and rehabilitation of stroke survivors, unfortunately is often unrecognized and underdiagnosed. The aim of this study was to estimate the prevalence and associated factors of PSD in two secondary hospitals in Cameroon

Methods:: This was a cross-sectional study including all stroke survivors who were at least 2 weeks post the event with good verbal communication. Stroke survivors with pre-existing depression, mental illness and those with post-stroke aphasia were excluded. The presence and severity of depression was measured using the Patient Health Questionnaire 9 (PHQ-9). Impairment in activities of daily living was assessed with the Barthel's Index.

Results:: Of 68 participants, males predominated (sex ratio: 1.13). Mean age was 59.76 (SD= 11.51 years). Majority of strokes were ischemic (n=49: 72.1%) and just over half (n=17: 54.8%) of those with PSD were within 3 months of onset of stroke. The prevalence of PSD was 45.6% (95% CI: 33.5%-58.1%), with a higher proportion in females (n=16: 50%) than males (n=15: 41.7%), (not statistically significant). One third of those with PSD had thoughts of self-harm or suicide. Impairment in activities of daily living was the only associated factor, significantly associated with PSD (p<0.001). There was no association between socio-demographic as well as the types of stroke and time since stroke and occurrence of PSD.

Conclusions:: The prevalence of post stroke depression is high and is strongly associated with impairment in activities of daily living.
LALLEMANTIA ROYLEANA BENTH MEDIATE ANXIOLYTIC LIKE EFFECT VIA MODULATION OF IONOTROPIC GABAA AND 5HT1A RECEPTOR TRANSMISSION: POSSIBLE MECHANISM OF ACTION

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Background and Aims:: Lallemantia royleana (Lamiaceae) is a part of Iranian folkloric medicine to treat various ailments, including mental illnesses. The aim of this study was to evaluate the anxiolytic-like and sedative effects of methanolic extract of L. royleana Benth. seeds (MeLRS) in NMRI male mice.

Methods:: MeLRS (75, 100, 250 and 500 mg/kg) was orally administered for seven days before subjecting to the behavioral battery of test for anxiety, Diazepam (DZP; 1 mg/kg, p.o.) and Buspirone (BUSP; 10 mg/kg, p.o.) were used as reference drugs. Mechanism of anxiolytic-like effect was also evaluated. Later, neurotransmitter analysis of GABA and monoamine was performed.

Results:: MeLRS was found to be non-toxic. Repeated oral administration MeLRS at (100 and 250 mg/kg) significantly increased time spent in open arm percent (TOAP) and entries in open arm percent (EOAP) in elevated plus maze paradigm (EPMP) as compared to vehicle (VEH) and similar to those observed in DZP and BUSP. Furthermore, MeLRS did not affect spontaneous locomotor activity. GC-MS analysis revealed linalool (27.2, 39.8%) mannitol (27.8, 14.78 %), glycerol (12.2, 10.43%) among monoterpene alcohol, sugars, and fatty acids. Pre-treatment with flumazenil (FLZ; 3mg/kg, i.p.)

Conclusions:: Results showed the significant anxiolytic-like effect of MeLRS and confirmed the traditional use L. royleana seeds as anxiolytic agent via activation of 5-HT1A and ionotropic GABAergic benzodiazepine receptors. These effects are mediated by modulation of GABA and monoamine neurotransmitter.
Background and Aims:: Apathy is a prevalent and disabling syndrome after traumatic brain injury (TBI), yet mechanistic understanding of apathy remains poor. This research examined the ability to process intrinsic (e.g., enjoyment) and extrinsic (e.g., money) reward underlying apathy after TBI.

Methods:: The study included 71 individuals with TBI (subdivided into with-apathy (TBI+A) and without-apathy (TBI−A) groups) and 41 demographically matched healthy controls. Participants completed a computerised task in which they decided whether to go to collect gifts ('go' option) or wait for the identical gifts delivered to their house ('wait' option). After this first section for intrinsic reward, a questionnaire was given to assess their evaluation on each option. In the second section for extrinsic reward, the procedure was the same, but with extra money given when participants chose to 'go' instead of to 'wait'. Throughout the task, a higher number of 'go' decisions indicated better performance.

Results:: For intrinsic reward, similar performance was observed in people with TBI+A, TBI−A and controls (p=.36, η^2=.018). However, the TBI+A group had a significantly higher percentage of people rating the "go" option as effortful compared to the control group (p=.01, w=.37). For extrinsic reward, the TBI+A group had the worst performance, then TBI−A, and control groups performing the best (p<.001, η^2=.194).

Conclusions:: For the first time, dysfunctional intrinsic and extrinsic reward processing underpinning apathy was demonstrated through TBI. This highlights the importance of strategies that tackle reward processing abnormalities in interventions and management of apathy in clinical practice.
PREMORBID PERSONALITY IN THE FRONTOTEMPORAL DEMENTIA - AMYOTROPHIC LATERAL SCLEROSIS SPECTRUM

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Background and Aims:: Frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) are recognized as part of the same neurodegenerative continuum (FTD-ALS spectrum). Factors determining phenotypic expression are unknown. However, it is common observation that personality differs between phenotypes: ALS patients often display a pleasant and nice attitude, while FTD patients frequently exhibit antisocial behaviors and lack of empathy. We therefore aimed at testing if FTD and ALS patients have different premorbid personalities, assuming that they reflect different vulnerabilities in brain circuits related to social behavior and motor function.

Methods:: We prospectively recruited patients presenting to our Memory and Motor Neuron Disease Clinics between December 2018-December 2020. Patients’ personality was assessed through the NEO Personality Inventory 3 (NEO-PI-3), which evaluates five domains (Neuroticism, Extraversion, Openness, Agreeableness, Conscientiousness). NEO-PI-3 was administered to caregivers with reference to patient’s personality at two timepoints: at diagnosis and 15 years prior to symptoms onset. Differences in personality factors between groups at each timepoint were tested with ANOVA.

Results:: 46 patients (30 FTD, 13 ALS, and 3 FTD-ALS assigned to the FTD or ALS group, based on first symptom) were recruited. A significant difference emerged in the Openness domain, showing that ALS patients (mean value 153±15) had been more open to experience, ideas and emotions than FTD patients (132±21, p=0.049).

Conclusions:: We found that premorbid personality differed among groups in at least one domain (Openness), supporting the hypothesis that premorbid personality may represent a vulnerability marker to the development of behavioral or motor disturbances. Our finding needs to be further explored with imaging.
IMPAIRMENT OF BIMANUAL MOVEMENT ON THE WAY TO RECOVERY FROM FRONTAL LOBE TUMOR SURGERY

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Background and Aims: The mechanism of bimanual coordination has not been fully elucidated. Here we evaluated the clinical features of bimanual movement impairment in frontal lobe tumor after respective surgery.

Methods: An elderly male patient with brain tumor in the right superior frontal gyrus was investigated. Five days previously he underwent subtotal resection which was histologically diagnosed as malignant lymphoma diffuse large B cell type, and subsequently receiving high-dose methotrexate based chemotherapy. After surgery he showed difficulty in bimanual movement that could not be attributable to weakness. Temporal change in characteristics of manual movement was analyzed.

Results: Bimanual diadochokinesis (opening / closing of hands, pronation / supination of forearms, and sequential movement of fingers) was more disturbed than unilateral hand movement of the same task. Both in-phase and anti-phase movements were impaired. Performance of bimanual movement was better when cued by auditory metronome. After ten days, these movements were improved.

Conclusions: Besides disturbance of anti-phase bimanual movements, resection of the frontal lobe involving the supplementary motor area can cause transient impairment of in-phase bimanual diadochokinesis. Effect of auditory cueing on bimanual skill is possibly useful for diagnosis and rehabilitation patients with brain tumor, as in the case of degenerative movement disorders.
ASSOCIATION BETWEEN LIPID PROFILES AND COGNITIVE FUNCTION IN TYPE 2 DIABETES MELLITUS PATIENTS

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Background and Aims: Type 2 Diabetes Mellitus (T2DM) remains a significant major health problem with several complications, including cognitive impairment. Modifiable risk factors affecting cognitive function in T2DM are various and still needed to be elaborated further, especially in people aged below 60 years, such as dyslipidemia. This study aimed to determine the association between lipid profiles and cognitive function in patients with T2DM.

Methods: This study was a cross-sectional study using consecutive sampling technique, at Endocrinology clinic General Hospital Haji Adam Malik Medan, from October to December 2020. All patients underwent laboratory examination to measure lipid profile levels, including total cholesterol, triglyceride (TG), HDL-C and LDL-C. Cognitive function was assessed using visual cognitive assessment test Indonesian version (VCAT-Ina)—a visual-based tool that is suitable for multicultural, multilingual society like in Indonesia.

Results: This study included 30 patients consisted of 16 females (53.3%) and 14 males (46.7%) with a mean age of 51.20±6.34 years. The mean of lipid profile levels were 194±46.6 mg/dl, 188.33±107.8 mg/dl, 36.73±10.6 mg/dl, 139.10±49.5 mg /dl, for total cholesterol, TG, HDL-C and LDL-C, respectively. The mean VCAT-Ina score was 21.63±2.69. Most of the patients (60%) were in MCI category. There were significant association between cognitive function with total cholesterol (p=0.006), TG (p=0.024) and LDL-C (p=0.012), but not with HDL-C (p=0.955).

Conclusions: Lipid profiles are significantly associated with cognitive function in T2DM patients. These results suggest that dyslipidemia should be addressed and may serve as an additional treatment target to prevent cognitive decline in T2DM patients.
SYNBIOTIC EFFECT OF PROBIOTIC COMPLEX WITH POLYPHENOLS COMBINATION FOR TREATMENT OF VALPROIC ACID-INDUCED PRENATAL MODEL OF AUTISM

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Background and Aims:: Gut Dysbiosis contributing to major pathogenesis in autism, there is a possible connection between the GI microflora and behavioral abnormalities. microbiota-gut-brain-axis is the ability of gut microbiota to communicate with the brain and regulate behavior. To improve these conditions modulation and daily supplementation of useful probiotics are needed.

Methods:: To the pregnant rats on Embryonic day 12 administer a single dose of valproic acid at 400mg/kg intraperitoneally. After weaning offspring on 7th-day rats with autistic features were separated for study and divided into groups. Treatment groups were daily supplemented with probiotic complex with Polyphenols and their combinations for the duration of Postnatal day (PND 8-50). During the treatment days, rats were assessed for various behavioral abnormalities. On PND50 rats were euthanized for biochemical analysis and Histopathological examination. All the experimental procedures were performed between 1.30 to 4.00 pm daily to maintain circadian rhythms.

Results:: Many born rats exhibited autistic features. Treatment with Probiotic complex with polypHENols alone and combination effectively reversed the autistic behaviors observed in Negative geotaxis, T-maze, Morris water maze, Social interaction, Repetitive Behavior. Biochemical alterations were recovered such as IL-6, TNF-α, BDNF, 5-HT, AchE as compared with the autistic group. Along we observed restoration of areas of the cerebellum like the Molecular layer and the Granular layer and they were looking normal.

Conclusions:: It is emphasized that the Probiotic complex with Polyphenols is synergetic, their combination augments the modulation of the dysbiotic gut, supports the Gut-Brain-Axis and this combination provides diversified benefits suitable to treat autism.
DOES NEUROCOGNITION FUNCTIONING IMPACT DRIVING HABITS IN OLDER ADULTS WITH HIV?

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Background and Aims:: Nearly 30%-50% of people living with HIV (PLWH) have HIV-Associated Neurocognitive Disorder. With half of PLWH being 50 and older, concerns mount that the prevalence and severity of neurocognitive impairment will increase with age. Yet, neurocognitive functioning can impact driving safety in older adults, but may also impact driving in older PLWH. Impairment in the neurocognitive domains utilized in driving may put PLWH at risk for decreased mobility that impacts their treatment adherence and quality of life. This study is the first to examine the driving habits of PLWH 40+ years and determine whether impairment in particular neurocognitive domains are predictive of driving habits.

Methods:: A sample of PLWH (N=260) were administered comprehensive norm-based neurocognitive tests and a measure of self-reported driving habits

Results:: While 166 (63.60%) participants possessed a driver’s license, 213 (81.61%) reported currently driving. Participants with a driver’s license had higher global neurocognition as well as better neurocognitive functioning in speed of processing and working memory. Participants with poorer neurocognition self-reported driving fewer miles. Those with more driving experience exhibited better neurocognitive functioning in global neurocognition, speed of processing, motor function, verbal fluency, working memory, and executive function. Participants who self-rated their driving as good/excellent demonstrated better neurocognitive abilities in global neurocognition, speed of processing, executive function, motor function, and verbal fluency.

Conclusions:: Neurocognitive functioning among older PLWH was associated with self-reported driving habits. Furthermore, neurocognitive functioning’s impact on driving can hinder PLWH’s access to medical care. Implications for public health, clinical practice, and research are posited.
NEUROPROTECTIVE POTENTIAL OF CHEBULIC ACID IN Aβ (1-42) INDUCED MODEL OF AD; TARGETING MITOGEN ACTIVATED PROTEIN KINASE

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Background and Aims:: Stress activated protein kinases such as p38 MAPK have been implicated in the pathogenesis of AD. The present study was designed to investigate neuroprotective mechanisms and therapeutic effect of chebulinic acid (ChA) in ICV-Aβ induced oxidative/nitrosative stress, neuroinflammation and alteration in neurochemistry resulting in cognitive deficits via p38 MAPK.

Methods:: Aβ 1-42 peptides at the dose of (3nmol/3 µL) twice on day 0 were infused bilaterally (ICV) after surgery to male wistar rats to induce dementia. ChA (25, 50 and 100 mg/kg/p. o) administered from 7th day onwards up to 21st day following Aβ infusion. The MWM and ORT were applied to measure learning and memory performance in animals. On day 22, following the behavioral tests, all the rats were sacrificed for evaluation of molecular alterations.

Results:: Rat with ChA, showed higher performance in MWM and ORT than rats treated Aβ whose memory performance declined compared to sham group. In addition, an elevation in neuroinflammatory cytokine (IL-1 β, IL-6 and TNF- α), p38 MAPK, Aβ levels and decrease in AchE and monoamines neurotransmitters (DA, Nadr, 5-HT, GABA and glutamate) was observed with Aβ injection. ChA reversed Aβ -triggered cognitive and molecular alterations.

Conclusions:: Results of the present study have thus demonstrated the role of p38 MAPK in cognitive deficit, cholinergic hypofunction, increase in oxidative-nitrosative stress and neurochemicals and histological alterations following Aβ infusion. To sum up, we can say that the healing effect of ChA on Aβ induced neurodegeneration opens a new door for the development of AD treatment.
PSYCHOLOGICAL IMPACT OF COVID-19 PANDEMIC ON MEDICAL STUDENTS IN SUDAN, 2020

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Background and Aims:: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an emerging infection causing a widely spread pandemic of (COVID-19). The current COVID-2019 pandemic is prompting fear of falling sick, dying, helplessness and stigma so urgent and timely understanding of mental health status is needed to help the community.

Methods:: A cross-sectional descriptive research was done among medical student in Sudan during COVID 19 pandemic in August 2020. DASS-21 scales were used to determine the level of depression, anxiety and stress among medical students through an online questionnaire, their responses were taken relatable to 21 items of DASS scale. The data was analyzed by means of SPSS version 25.0.

Results:: The mean (SD) age of our study participants was 21.8 (2.4) with female to male ratio of 2.1. Interestingly, more than 40.5% of the study participants were free of depression while more than 13% had extremely severe depression. On the other hand, only 4.4% had extremely severe stress. However, anxiety ranked the higher numbers with 23% had extremely severe anxiety. Adjusted linear regression model revealed that lower levels in the medical school and open colleges during the lock down period were associated with more anxiety (p value 0.01,0.006 respectively).

Conclusions:: It's important to support high-risk groups especially those with preexisting mental illness to offer advanced psychological interventions. So our study can be used to construct and formulate a psychological intervention and implement mental health strategies directed toward vulnerable groups during the COVID-19 epidemic.
BRAIN TARGETED POLYMERIC NANOPARTICLES OF ALENDRONATE CONFERS IMPROVED PHARMACOKINETIC AND NEUROPROTECTIVE EFFECT AGAINST ALZHEIMER’S DISEASE LIKE PATHOLOGICAL CHANGES IN HIGH FAT DIET FED MICE

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Background and Aims:: Increasing prevalence of Alzheimer’s disease (AD) has presented it as one of the major neurodegenerative disorder worsening the quality of life of elderly. AD is one of the complex forms of dementia which is affecting millions of people. AD is a progressive neurodegenerative disorder with short-term memory impairment, successive cognitive disabilities, Aβ deposition, neurofibrillary tangles, neuronal death. The unclear etiology and lack of therapy reveals an urgent need to investigate the potential therapeutic approaches. Furthermore, alendronate (bisphosphonate) was cited to exhibit neuroprotective role by modulating the components of Mevalonate pathway. Thus, the present study was designed to develop the brain targeted polymeric nanoparticles of alendronate (ALN-NPs) to overcome its side effects and poor pharmacokinetics and to investigate its effect against high fat diet (HFD)-induced AD-like pathological symptoms in mice.

Methods:: ALN-NPs were developed using ionic-gelation technique and characterized for particle size, TEM, SEM, in-vitro, ex-vivo release, pharmacokinetic profile. The optimized ALN-NPs were administered intranasally in mice to deliver ALN to brain following investigation against neurobehavioral, neurochemical (β-secretase, Aβ, neuroinflammation, isoprenoids, GSK-3β, oxidative stress) and histopathological changes (Aβ deposition).

Results:: The developed ALN-NPs acquired the particle size within 200nm along with improved pharmacokinetica. Additionally, ALN-NPs were found to alter remarkably the HFD-induced neurobehavioral, neurochemical changes and reduced Aβ in mice hippocampus. ALN-NPs also reduced the hippocampal isoprenoids level in mice which corresponds to the reduced AD-like symptoms.

Conclusions:: Our current outcomes suggest the prominent role of ALN-NPs against AD-like pathologies by targeting Mevalonate pathway, supporting this bone drug a potential target for AD treatment.
ANALYSIS OF COGNITIVE DISORDERS ON INTERNET GAMING DISORDER (IGD) PATIENTS IN RURAL AREA OF YOGYAKARTA, INDONESIA

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Background and Aims:: Internet Gaming Disorder (IGD) phenomenon arises due to the inability of controlling internet usage and its related contents. The prevalence of IGD tends to arise (0.3%-10.8%). In 2016 World Health Organization (WHO) informing that IGD was part of gaming disorders in ICD-11. IGD was one condition that may affect cognitive status. This condition may happen due to long hours of internet usage, including playing games. This study aims to analyze the cognitive disorders of junior high school students with IGD in the rural area of Yogyakarta, Indonesia.

Methods:: This study was using an observational analytic design with a cross-sectional approach towards junior high school students. The respondents were divided into two groups (students with IGD and without IGD) containing 37 respondents each. Both groups performed cognitive status examinations using MMMSEC-Ina. Analysis of the cognitive status of both groups includes the diagnosis of IGD, the types of games, and the duration of internet usage with Mann Whitney test followed by linear regression test.

Results:: From the results, the Mann-Whitney test results on cognitive status showed a trend of decreasing the average cognitive value of each domain, especially the calculation/attention domain p = 0.000; and cognitive total p = 0.029. Bivariate correlation test results with outside variables were not found to be significant. The multivariate test results showed that IGD was significantly correlated with cognitive status with B = 1.293; p = 0.024.

Conclusions:: Patients with IGD in the rural area of Yogyakarta experience cognitive dysfunction, especially in the domain of calculation or attention.
PREVALENCE, CLINICAL CHARACTERISTICS OF HEADACHE IN MEDICAL STUDENTS AT ALZAIEM ALAZHARI UNIVERSITY IN 2020, KARTOUM, SUDAN

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Background and Aims:: Headache is one of the most common disorders of the nervous system. Headache means pain in the head. The (WHO) reports that almost half of the adults worldwide will experience headache in any time at any given year. The study aims To determine the prevalence rate and clinical characteristics of headache among medical students in Alzaiem Alazhari university in Khartoum state, Sudan in 2020.

Methods:: A descriptive cross-sectional study using a 41 items questionnaire was introduced to 71 medical students from Alzaeim Alazhari university in the period from January 1st to 15th of February.

Results:: Out of the 71 respondents 35 (49.3%) were Male and 36 (50.7%) were female while most of them were in the (21-24) age group by (69.01%). Most of the participants responded that they headaches (74.65%) with (32.31%) of them having continuous and (67.69%) of them with no continuous headache. 32 (45.07%) of them had headaches, half of them lasted for 1-2 hours and the other half lasted more than 10 hours per day. The most common location for the headache was both sides (23.02%) followed by the forehead (22.22%). The most common characteristic of headache was pulsating (48.48%) followed by pressure like (37.88%).

Conclusions:: There is a high prevalence rate of headache among medical students with migraine as the most common cause of headache.
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Background and Aims:: Recent studies indicate the coexistence of migraine and restless leg syndrome (RLS). This correlation cannot be attributed to one single mechanism. A possible hypothesis might be the dopaminergic dysfunction in the hypothalamic nuclei in both of these entities.

Methods:: We present a 56-year-old female patient who presented to our outpatient clinic with recurrent episodes of headache that fulfilled the criteria of migraine without aura (ICHD-3 criteria). Because of the frequency of the episodes the patient was put on prophylactic treatment with topiramate. One month after treatment initiation her symptoms were improved, regarding both the duration and the intensity of the pain. Four months after her first visit she complained for dysesthesia of her lower limbs, accompanied by an urgent need to move them, especially at night and improvement of these symptoms with movement. The investigation made to exclude other causes that could cause these symptoms was negative. Pramipexole was initiated in order to treat RLS.

Results:: The migraine attacks were diminished after one month treatment with pramipexole. The last twenty days the patient experienced no pain at all. The discomfort from her lower limbs disappeared too.

Conclusions:: The beneficial action of pramipexole to our patient and the further relief of her migraine attacks can be attributed to the improvement of her sleep. Furthermore, past studies suggest impairment in dopamine synthesis in patients with migraine. Pramipexole – a dopamine agonist – could be involved in this therapeutic path too.
HYPEREXCITABILITY AND DYSFUNCTION OF CORTICAL EXCITATION / INHIBITION MECHANISMS IN MIGRAINE: A PAIRED PULSE TMS STUDY

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Background and Aims: Paired-pulse TMS paradigms can be used to test connectivity within the primary motor cortex. Aim of the study was to provide additional information on short intracortical inhibition (SICI) and intracortical facilitation (ICF) using different intensities of the test stimulus (TS) in episodic and chronic migraine (CM, EM) patients.

Methods: We enrolled 24 patients with EM, 13 with CM and 24 healthy subjects. EM and controls were randomly assigned to two groups for assessment of SICI and ICF. While in patients with CM we tested both ICF and SICI during the same experiment. We assessed SICI and ICF at three different suprathreshold intensities of the TS (110%, 130% and 150% of the resting motor threshold). Interstimulus intervals of 2 ms and 10 ms were used for testing SICI and ICF respectively.

Results: When testing ICF, maximum increase in conditioned MEP amplitude was observed in EM at the lower stimulation intensity of the TS (p<0.005). This intensity was indeed to induce significant facilitation in the CM and healthy subjects. No significant differences were observed as regards SICI.

Conclusions: Our results strengthen the notion of altered tuning of cortical excitability in migraine. The increased ICF cannot be detected at higher stimulation intensities in EM probably due to the induction of homeostatic regulatory mechanisms of cortical excitability that could aim to protect against the risk of neuronal damage. CM have a greater cortical excitability than EM and the homeostatic regulatory mechanisms of cortical excitability are activated early, even at 110% of TS.
A NOVEL SCORING APPROACH TO IDENTIFY RESPONDERS TO ERENUMAB IN CLINICAL PRACTICE

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Background and Aims:: In clinical practice, a successful therapeutic response depends not only on a 50\% reduction in migraine days, but also on improved migraine symptoms severity and patients’ disability. In this study, we aimed to develop a multidimensional composite score that combines measures that are clinically relevant to establish migraine patients’ response to erenumab.

Methods:: The primary outcome of the study was erenumab efficacy, established following standard clinical evaluation. A composite treatment response score was calculated as a linear combination of response criteria evaluating significant changes in migraine frequency, headache frequency, severity of the migraine attack and migraine-related disability. Logistic regression models were run to assess the association of the composite response score, as well as different response criteria, with the primary efficacy outcome. The Brier Score and receiver-operating characteristic (ROC) analyses were performed to assess model discriminative ability.

Results:: Thirty-eight (53\%), 42 (68\%) and 24 (73\%) patients achieved the primary efficacy outcome after 3, 6 and 12 months of erenumab, respectively. The composite response score achieved the lowest Brier scores at each time point, suggesting a higher predictive accuracy. Compared to the other response criteria, the composite response score had the highest AUC values at month 3, month 6 and month 12.

Conclusions:: Here, we proposed a simple and exhaustive multidimensional score that is reliable and stable to follow-up migraine patients’ treatment response over time. The use of a simple and comprehensive score may facilitate patients’ management in clinical practice and may expand patients’ access to effective therapies.
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Background and Aims:: Trigeminal neuralgia is a disorder characterized by agonizing facial pain paroxysms which are triggered by innoxious ordinary activities. It is noted to be more prevalent in females and in ages >50 years. Aims: To outline the clinical profile in patients with trigeminal neuralgia and define the management protocols under use.

Methods:: Cross-sectional, analytical, hospital-based study including 45 patients enrolled from three neurology outpatient clinics and the pain management centre- Khartoum State- Sudan during October 2020- February 2021. Semistructured questionnaire was used for data collection, different statistical parameters were calculated and P-value of <0.05 was considered as significant.

Results:: Female predominance was noted (64.4%) with mean age of disease onset being 48.04 ± 12.79 years. Patients’ first presentation was in dental and general medical clinics (77.8%) and the mean diagnostic delay was 44.24 ± 43.24 months. Acute attacks were affecting the right facial side (53.3%) at areas of both maxillary and mandibular divisions (37.8%), having trigger zones (64.5%) and triggering factors (86.7%) with associated autonomic features (8.9%) and facial spasm (2.2%). Persistent dull pain was mentioned by 57.8% of the patients. Treatment was based on carbamazepine either as daily regimen (71.1%) or interrupted courses (28.9%) with add-on procedures performed to 24.4% of the patients. Significant correlations were found between the treatment regimen and the clinical profile as well as the diagnostic delay time.

Conclusions:: Patients’ demographics and clinical profile were coinciding with the previously published data. Variable treatment modalities are available and the period of diagnostic delay significantly affects the protocol to be used.
EVALUATION OF PSYCHOLOGICAL PREDICTORS OF REAL-LIFE EXPERIENCE WITH ERENUMAB IN CHRONIC MIGRAINE WITH OR WITHOUT MEDICATION OVERUSE: DATA FROM A 1-YEAR FOLLOW-UP

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Background and Aims:: To evaluate the psychological predictors of the outcome of real-life experience with the anti-CGRP monoclonal antibody Erenumab in a 1-year follow-up in chronic migraine (CM).

Methods:: Seventy-one patients (age: 49.1 ± 9.5, F: 72%) with CM+MO (ICHD-III criteria) who had already failed at least two preventive therapies received Erenumab (70 or 140-mg dose s.c.). At T0 patients received also a full psychological evaluation comprising mood, anxiety, and personality disorders as well as alexithymia traits, childhood traumas and current stressors. They were followed up at 1 year for their clinical condition.

Results:: At the 1-year follow-up, 50 patients (mean age:49.0 ± 9.5) reported a reduction of at least 50% in migraine days/month (Responders, R); whereas 21 (mean age:49.3 ± 9.7) did not (non Responders, NR). When compared to R, NR were characterized by a higher prevalence of anxiety (90% vs 60%, p=.012) and Cluster C (avoidant, dependent, and obsessive-compulsive) personality disorders (87% vs 38%, p=.002). They also showed more alexithymic traits (53.2 ± 12.9 vs 43.7 ± 14.2, p=.03) and a higher number of stressors (1.2 ± 2.5 vs 0.3 ± 0.7, p=.012). The two groups were similar for mood disorders and childhood traumas.

Conclusions:: Erenumab is an effective option for patients with difficult-to-treat migraine. These patients are often characterized by relevant psychological comorbidities. Our findings, even if preliminary, show a further distinction within difficult-to-treat CM+MO patients, highlighting the impact of current stressors, anxiety and an “anxious-fearful” personality in those patients being refractory to many preventive treatments, including Erenumab.
Background and Aims:: Alexithymia is a personality trait characterized by the inability to identify and express emotions. Several studies evidenced a positive association between alexithymia and psychological distress in patients with chronic migraine (CM) and fibromyalgia (FM). Here we evaluated the prevalence of alexithymia and distress in FM and CM, compared to healthy controls (HC).

Methods:: Two-hundred and fifty women with CM (mean age: 46.1 ± 11.5, disease duration: 7.9 ± 7.3yrs) and 250 FM (mean age: 51.2 ± 10.5, disease duration: 7.9 ± 7.8yrs) were assessed by the Toronto Alexithymia Scale (TAS-20), and the Hospital Anxiety and Depression Scale (HADS). A HC group (n=280; mean age: 51.8 ± 9.0) was also enrolled and assessed by TAS-20 and HADS.

Results:: Differences between groups showed significantly higher levels of alexithymia [F(2,755) = 11.7, p < .001] and psychological distress in FM patients [F(2,763) = 31.7, p < .001], compared to CM and HC. Post-hoc analysis showed that CM patients reported higher levels compared to HC group in the total score (p < .001) and in the Difficulty Identifying Feeling subscale of the TAS-20 (p < .001). A moderation analysis was performed to examine the moderation effect of the group (CM vs. FM) on the relationship between alexithymia and psychological distress. Besides a strong relationship between alexithymia and distress, the group variable was not a significant moderator.

Conclusions:: These findings might suggest a common psychological dysregulation in patients suffering from chronic migraine and fibromyalgia, which manifests into a different expression of the physical symptom.
Background and Aims:: Lifestyle, behaviours, physical activity (PA) and working habits had been influenced by COVID-19 lockdown. Aim of the study is to assess the impact of lockdown on migraine.

Methods:: Migraineurs who attended the Headache Centre from 01.06.2019 to 31.12.2019 were interviewed. Patients were prophylaxis free or they were on the same prophylaxis from at least 3 months. Demographics, working routine, lifestyle, migraine characteristics and disability (HIT-6) were compared between the first month of the lockdown (March 2020) and a reference month prior the lockdown (January 2020).

Results:: Thirty-seven patients were analysed in two groups, migraine without aura (MwoA) (n=26, 45 y [31-53]) and migraine with aura (MwA) plus migraine with and without aura (MwA/MwoA) (n=11, 38 y [26-47]). No changes were reported for food/fluid/alcohol intake, smoke and sleep, while PA decreased (65% vs 31%; p=0.012). Time spent working outside the habitation reduced (MwoA, p=0.001; MwA plus MwA/MwoA, p=0.005) with an increase of remote working (MwoA, p=0.011; MwA plus MwA/MwoA, p=0.039). Patients with MwoA reported mean headache duration [3h, (2-12) vs 2h (1-8); p=0.041] and HIT score [59 (51-63) vs 50 (44-57); p=0.001. Patients with MwoA living in urban area had a higher HIT score than those living in rural area [53 (46-57) vs 42 (36-49) (p=0.033)]. Severity of the attack and symptomatic drug intake didn't change.

Conclusions:: Pain duration and disability improved in MwoA during lockdown, probably due to possibility to rest during attack. Living in rural area might have a protective role.
HEADACHE DURING COVID-19 FIRST WAVE: A STUDY ON HEADACHE ADMISSIONS AND “REPEATER” MIGRAINEURS IN EMERGENCY DEPARTMENT

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Background and Aims:: During the first Italian COVID-19 lockdown a reduction in Emergency Department (ED) attendances due to non-SARS COV2 related acute/chronic neurological diseases was observed. The aim of this study was to analyze the influence of COVID-19 outbreak on total ED admissions due to headache as the principal presenting symptom and on “repeater” migraineurs

Methods:: We retrospectively evaluated frequency, features and management of ED attendances for headache in the tertiary-care University Hospital of Trieste during the lockdown period (from 8th March to the 31st May 2020) comparing it with the pre lock down period (January-February 2020) and the first five months of 2019.

Results:: A reduction of all headache ED attendances was observed in the first five months of 2020 compared to the same period of 2019 (174 and 339 respectively; -49%). During the lockdown only a reduction of female ED access rate (p= 0.03) was found, while no significant variation was detected in repeaters prevalence, diagnostic assessment, and acute treatment. The ratio of Not Otherwise Specified (NOS), Secondary and Primary Headaches remained unchanged during the lockdown period, in comparison to control periods. NOS headache remained the most frequent discharge diagnosis (48.4%), followed by Primary and secondary headache (21.0% and 30.6 %).

Conclusions:: COVID-19 pandemic impacted the number of ED attendances for headache but not their management and discharge diagnosis distribution. A quote of secondary dangerous headaches did not arrive to ED, while a portion of repeaters continued to refer to ED despite COVID-19 lockdown.
HEADACHE WITH FILLING OF THE BLADDER AS ONE OF THE VARIANTS OF PRIMARY HEADACHES

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Background and Aims:: There are many types of primary headaches such as cold headache, postcoital headache, and others.

Methods:: At the reception, 3 patients were examined with a headache during filling of the bladder. The sex of all patients was male. Age 26, 30 and 40. no concomitant pathologies were identified. The duration of headaches is 5, 3 and 6 years respectively. In patients, the nature of the headache was of a pulsating, burning character, periodically there was nausea during the headache. The pain is localized on half of the head and it lasts until the act of urination. After urination, as a rule, the pain stops or decreases, rarely the pain lasts until the end of the day. In one patient, this condition appeared after receiving craniocerebral trauma. Laboratory analyzes of urine and prostate without pathology. MSCT of the abdominal and pelvic cavity was normal. Sonography, Cystoscopy of the bladder was without pathological changes. urologist excludes diseases of the urinary system. MRI of the brain without any significant changes, no pathological waves were observed on the EEG.

Results:: The patient was prescribed treatment according to the standard as a primary headache: NSAIDs, as a preventive G. B. antidepressant drugs. Inspection after 3 and 6 months is recommended. During repeated examinations headache are not marked. Improvement of symptoms in dynamic.

Conclusions:: Conclusion: In this patient's example, primary headaches have a very variable clinic. It is possible to consider G.B. when urinating, one of the options for primary GB, as a postcoital headache.
Background and Aims:: Headache disorders have a strong impact on sufferers' lives; however, the “content” of assessment instruments addressing concepts, such as disability and quality of life (QoL), is poorly defined. The aim of the present review is to provide information on the content coverage of the most commonly used assessment instruments (for disability, QoL or work-related difficulties) in primary headache disorders.

Methods:: We searched SCOPUS for research papers in which outcome measures were used in adult populations of patients with migraine, tension-type headache (TTH), and cluster headache (CH). The content of single instruments was then mapped against the International Classification of Functioning, Disability, and Health (ICF).

Results:: A total of 150 papers and 26 instruments were included: 15 addressed disability or impact, 2 addressed work-related difficulties, and 9 addressed QoL. Few instruments (e.g. the MIDAS, the HIT-6, and the SF-36) were commonly used across the conditions and covered domains of functioning such as: impact on daily life activities, homework, school, and work-related tasks, leisure time, informal and family relations, pain, emotional difficulties, energy level, and impulse control.

Conclusions:: Most of the research is based on instruments that poorly acknowledge the role of environmental factors and the impact of headache disorders on work-related activities. Moreover, most of the measures were developed for migraine, which is critical for CH. Further research is needed to expand the scope of measures exploring headaches impact on daily life activities, and to raise knowledge on the less represented areas, e.g., TTH impact.
EXTENSIVE CEREBRAL VENOUS THROMBOSIS SECONDARY TO ESSENTIAL THROMBOCYTHEMIA TREATED WITH LUMBO-PERITONEAL SHUNTING

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**Background and Aims::** Essential thrombocythemia (ET) is a myeloproliferative disease with megakaryocytic hyperplasia in bone marrow. Even though thrombo haemorrhagic complications are common in ET, cerebral venous thrombosis (CVT) is an unusual presentation. We describe a Sri Lankan female with severe CVT due to ET treated with lumbo peritoneal shunting.

**Methods::** Case Report A 35-year-old female presented with chronic headache for four months. Examination revealed papilledema without other focal neurological signs. She did not complain of visual obscurations or diplopia. MRI brain was normal. MRV confirmed severe CVT involving bilateral superior sagittal and transverse sinuses extending up to jugular bulb. A Lumbar puncture revealed CSF opening pressure of 330mm H2O and therapeutic removal of 30cc CSF was performed. She was started on oral acetazolamide and anticoagulation. However her symptoms persisted hence a lumbo peritoneal shunt was inserted, after which she made a significant recovery.

**Results::** FBC revealed thrombocytosis with normal haemoglobin level and WBC count. Bone marrow examination revealed megakaryocytic hyperplasia. These findings were in keeping with a myeloproliferative disease, essential thrombocythaemia. Genetic test for myeloproliferative neoplasm (MPN) was positive for JAK2p.V617F mutation. Rest of the thrombophilic screening was negative. Hydroxyurea was added as treatment.

**Conclusions::** CVT as the first presentation of ET is very rare with only a few cases reported in literature. This case emphasizes the need for extensive evaluation of patients with CVT in order to find an underlying cause. Lumbo peritoneal shunting is a treatment option in extreme cases of CVT. Ours is the first such procedure performed in Sri Lanka.
HEADACHE BURDEN IN A HIV POPULATION OF SUB-SAHARAN AFRICA

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Background and Aims:: About 26 million people are living with HIV in sub-Saharan Africa (SSA). The DREAM programme in SSA provides free healthcare for HIV/AIDS and a range of chronic non-communicable diseases. HIV is a risk factor for neurological disorders including stroke and epilepsy, which themselves are associated with headache, and HIV may be a direct risk factor for headache. We investigated the prevalence and burden of headache in a HIV+ population in SSA.

Methods:: At the DREAM Centre in Blantyre, Malawi, a low-income country with 18.5 million population and 9.2% HIV prevalence, a structured questionnaire was administered by a trained lay interviewer to consecutively attending HIV+ patients aged 18-65 years. All were monitored with regular viral load detection.

Results:: Of 513 eligible patients invited, 498 were included (15 declined; mean age 34.1±12.8 years; 72% females). All were on antiretroviral treatment (ART), with viral load undetectable in 83.9%. The 1-year prevalence of headache was 80.3% (females 83.6%, males 71.9%); 3.8% had ≥15 headache days/month, 1.4% had probable medication-overuse headache. Mean overall headache frequency was 4.4±5.4 days/month. Those reporting headache lost means of 2.7% of paid workdays and 3.9% of household workdays because of headache. Only a third had sought advice for their headache.

Conclusions:: Headache is very prevalent among HIV+ patients in Malawi, imposing additional burden and costs on individuals and the community. Management of headache disorders should be implemented in HIV centres, as it is for other chronic non-communicable diseases. The study was supported by Lifting The Burden and ANIRCEF
ENLARGING THE SPECTRUM OF CLUSTER HEADACHE: CAN VOICE ANALYSIS REVEAL AN EXTRACRANIAL AUTONOMIC INVOLVEMENT?

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Background and Aims:: Despite a well-characterized clinical phenotype, cluster headache (CH) is frequently burdened by misdiagnosis or diagnostic delay. In our experience, we noticed a typical voice quality with low and croaking tone in CH patients. We evaluated, by means of digital voice analysis, whether a typical voice quality characterizes CH patients when compared to healthy controls (HC).

Methods:: By means of an accurate, reproducible and feasible digital voice analysis, voice measures has been studied including the traditional measures of fundamental frequency, calculations of jitter and shimmer, and noise-to-harmonics ratios as well as quantities related to the spectral tilt (i.e., H1-H2, H1-A1, H1-A2, H1-A3) in 20 CH patients and in 13 matched healthy controls (HC). A video-laryngostroboscopy, was performed in all the subjects.

Results:: CH patients, explored during the cluster-bout period, showed a peculiar voice quality, the so-called creaky voice, characterized by lower values of H1-H2 in comparison with HC. By using a laryngoscopy investigation, bilateral mild to marked vocal cord oedema and signs of laryngo-pharyngeal reflux have been found in CH patients.
Conclusions: Creaky phonation is a “physiological normal mode of laryngeal operation” usually subtended by shortened and thickened vocal folds. Creaky voice phonation can be due to a reduced vocal folds capability to become slack or flaccid secondary to vocal cords oedema subtended by laryngo-pharyngeal reflux affecting the phonatory mechanisms in CH patients. The laryngo-pharyngeal reflux may represent a dysautonomic sign related to the increased parasympathetic tone during in-bouts period, reinforcing the hypothesis of an extracranial autonomic dysfunction as part of the CH clinical picture.
Background and Aims:: Idiopathic intracranial hypertension (IIH) is a well-established entity with increased intracranial pressure of unknown etiology. However, physicians are less aware of drug induced hypertension. Some of the commonly used medications in dermatology, especially those for acne vulgaris, have been associated with IIH. To our knowledge, only two cases of IIH reported in the literature have been associated with mesalasine treatment, which is a product of 5 aminosalicylate (5 ASA).

Methods:: Case report

Results:: A 51 year-old woman was admitted to our department with the complaint of headache and binocular horizontal diplopia. She had been on sulphasalazine treatment (2000 mg per day) for ulcerative colitis one year previously. Neurological examination revealed a bilateral sixth nerve palsy with bilateral papilledema. Brain MRI showed a partially empty sella with a distension of the optic nerve sheaths. Lumbar puncture (LP) revealed an opening pressure of 320-mm H2O with a normal cerebrospinal fluid composition. After elimination of other causes of intracranial hypertension, the diagnosis of IIH associated with sulphasalazine was suspected and this drug was accordingly discontinued. The patient was continued with azathioprine for ulcerative colitis and acetazolamide 750 mg/day with improvement of all the symptoms.

Conclusions:: Although the mechanism of intracranial hypertension associated with sulphasalazine treatment still unknown, it is imperative that clinicians recognise this causal relationship to prevent irreversible visual complications.
EFFECTIVENESS AND SAFETY OF CGRP-MABS IN MENSTRUAL RELATED MIGRAINE: A REAL-WORLD EXPERIENCE

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Background and Aims:: Migraine shows a higher prevalence in women especially during reproductive age. Over 50% of patients report a higher occurrence of migraine attacks during perimenstrual window. Menstrual migraine attacks are referred as more disabling, less responsive to symptomatic treatments, longer in duration, and more prone to relapse than non-menstrual migraine attacks. Several evidences suggest that estrogen fluctuations are involved in migraine attacks worsening during the perimenstrual window through several mechanisms involving CGRP pathway. We aimed to evaluate whether mAbs blocking CGRP-ligand or receptor (CGRP-mAbs) could represent an effective and safety preventive treatment for menstrual migraine attacks in patients with menstrual related migraine (MRM) with previous treatment failures.

Methods:: Forty patients with MRM with previous treatment failures received monthly CGRP-mAbs. At the baseline and after six CGRP-mAbs administrations, patients underwent to extensive interviews to assess frequency, duration, intensity and responsiveness to painkillers intake of migraine attacks during the perimenstrual window.

Results:: After 6 administrations of CGRP-mAbs we observed a reduction of median menstrual migraine frequency (from 5 to 2 days per month), pain intensity (from 8/10 to 6/10), attacks duration (from 24 hours to 8 hours) and a significant increase in the percentage of responding to painkillers (from 42.5% to 95%) (p<0.001).
Fig. 1
Conclusions:: CGRP-mAbs could represent a safety and effective preventive therapeutic strategy able to reduce the disabling burden of menstrual migraine attacks frequency, duration, intensity and significantly improve the response to painkillers. These findings could be related to and prove the greater influence of CGRP-mediated mechanisms in the pathophysiology of menstrual migraine attacks.
MANNITOL EFFECTIVENESS IN LOWERING INTRACRANIAL PRESSURE IN IDIOPATHIC INTRACRANIAL HYPERTENSION: A CASE SERIES

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Background and Aims:: Headache, transient visual loss, papilledema are the most frequent clinical features of idiopathic intracranial hypertension (IIH). If untreated, papilledema can result in progressive and irreversible vision loss. Mannitol is an osmotic diuretic commonly used to reduce high ICP in traumatic brain injuries, but its action in IIH is still unknown. Here we report effects of mannitol on CSF pressure in patients with IIH and papilledema.

Methods:: Four female with refractory headache and visual loss showing clinical, funduscopic and radiological signs suggestive of IIH were treated with intravenous infusion of mannitol 18% (0.6 g/kg, infusion speed: 125 ml/h) during continuous short-lasting CSF pressure recording through a spinal needle.

Results:: Mannitol administration stably normalized CSF pressure (<200 mmH2O) with abnormal waves disappearing and headache improvement in two out of four patients within 40’ and 45’. All four patients had evidence of: high opening (>250 mmH2O) and mean (>300 mmH2O) pressure and B-waves, papilledema and bilateral transverse sinus stenosis on cerebral-MR-venography. However, the two mannitol-responder patients showed all MRI signs (posterior sclera flattening, peri optic subaracnoid space distension, empty sella and optic nerve tortuosity) suggestive of IIH, whereas in the remaining two patients only the last two abnormalities were evident.

Conclusions:: We firstly report in vivo evidence of mannitol effect on CSF pressure in subjects with IIH. Mannitol normalized CSF pressure only in two subjects, in which more severe MRI signs of IIH were evident. Larger population study should be useful to confirm mannitol efficacy in IIH patients and to better identify predictor factors of mannitol efficacy.
WHOLE BRAIN SURFACE-BASED MORPHOMETRY STUDY IN SUBTYPES OF MIGRAINE WITH AURA PATIENTS

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Background and Aims:: Little is known about the pathophysiologic basis of the clinical variability of migraine aura presentation. We were aimed to study intracerebral white matter fiber bundles, using a tract-based spatial statistics (TBSS) analysis of diffusion tensor imaging (DTI), and grey matter cortical thickness from structural magnetic resonance imaging data in migraine patients with pure visual auras (MA), and in patients with complex neurological auras (MA+), i.e. with the addition of at least one of sensory and language symptoms.

Methods:: 3T MRI data from 20 patients with MA and 15 with MA+ were collected and compared with data from 19 healthy controls (HCs). For everyone, we performed DTI to calculate diffusivity metrics and we obtained cortical thickness maps from structural MRI.

Results:: TBSS showed no significant differences in the diffusivity maps between both patients’ groups and HCs. As compared to HCs, both patients with MA and MA+ significantly showed thinner temporal cortices, frontal areas, insula, post-central area, and primary and associative visual areas. In the MA group, the high-level visual-information-processing areas, including lingual gyrus, were thicker, in contrast to the MA+ group where they were thinner than in HCs.

Conclusions:: These findings suggest that clinical heterogeneity of migraine with aura is associated with common cortical surface morphological features as well as with an opposite morphological involvement of the high-level visual-information-processing areas.
A 67-YEAR-OLD WOMAN WITH RECURRENT HEADACHE, MIGRATORY FOCAL SYMPTOMS, AND IMPAIRED CONSCIOUSNESS

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Background and Aims:: We present the clinical story of a 67-years-old woman with a previous diagnosis of migraine with aura developing stereotyped episodes, lasting for several hours, of focal visual, sensorimotor and aphasic neurological symptoms, and altered state of consciousness associated with a headache with migraine features.

Methods:: We discuss a case report including an up-to-date review of all previous cases in the field. To apply the Popper’s conjectures refutation paradigm, we carry out a differential diagnosis evaluating the pros and cons of possible hypotheses to confirm or refute HaNDL syndrome diagnostic hypotheses. A written informed consent was obtained from the patient for description of this case report.

Results:: The neuroimaging finding ruled out the diagnosis of hemorrhagic or ischemic stroke. EEG non-epileptiform changes characterized by an asymmetrical generalized slowing and triphasic waves allowed to exclude the diagnosis of migraine aura triggered seizure with prolonged ictal state. CSF analysis showed a pleocytosis in the absence of fever, meningism and with negative microbiological investigations disavowed infective encephalitis/meningitis. The absence of neuronal antibodies in both CSF and plasma did not support the diagnosis of autoimmune encephalitis. Finally, blood laboratory tests made the plasma hyperviscosity syndrome improbable. Altogether these findings supported the diagnosis of transient headache and neurological deficit with CSF lymphocytosis (HaNDL).

Conclusions:: HaNDL syndrome is one of the most frequent “stroke mimicker” that should be taken into account in patients with recurrent episodes of acute, migratory and transient neurological symptoms not respecting a single vascular territory but probably reflecting a cortical spreading depression (CSD).

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Background and Aims:: Refractory migraine (Ref-M) represents a conundrum that headache experts have to face with. We aim to investigate whether a peculiar profile may characterize patients with Ref-M according to 2020 European Headache Federation criteria. Furthermore, to substantiate a dysfunctional dopaminergic pathway involvement in these patients, we explored the effectiveness of olanzapine.

Methods:: Eighty-four patients (fitting previous Ref-M criteria of the 2014) were treated with erenumab for six months. Differences between clinical and demographic features of responder (Ref-M according to 2014 criteria) and not-responder (Ref-M according to 2020 criteria) patients to CGRP-mAbs were investigated and their predictive values assessed. In fifteen patients with Ref-M not-responders to CGRP-mAbs, olanzapine was administered (5 mg/die) for 3 months and frequency and pain intensity of migraine attacks were estimated.

Results:: Patients with Ref-M not-response to CGRP-mAbs (29/84) when compared with Ref-M responsive to CGRP-mAbs showed higher baseline frequency of migraine attacks, medication overuse and pain catastrophizing scale (PCS) scores. Logistic regression analyses showed that frequency of attacks, medication overuse and PCS score represent independent negative predictors of CGRP-mAbs response. A ≥50% reduction of headache days/month was observed after olanzapine treatment in 67% of patients with Ref-M not-responsive to CGRP-mAbs.
Conclusions:: We outline that higher frequency of migraine attacks, medication overuse and pain catastrophizing characterize patients with Ref-M not responsive to CGRP-mABs. In this frame, olanzapine effectiveness on frequency and pain intensity of migraine attacks supports the hypothesis that migraine refractoriness may be subtended by a prominent involvement of the dopaminergic pathway.
SAFETY, EFFICACY AND SLEEP EFFECT OF ERENUMAB IN CHRONIC MIGRAINE: 12 MONTHS REAL LIFE DATA

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Background and Aims:: Erenumab, human monoclonal antibody directed against CGRP receptor, is first approved specific treatment for migraine. In this real-life study, we evaluate the efficacy and safety of erenumab associated with a multidisciplinary impact including sleep and circadian effect in 12 months treatment.

Methods:: Data are collected From Headache Center in Policlinico of Palermo and Messina, IRCSS Neurolesi Center "Bonino Pulejo". Patients with chronic refractory migraine received 140mg or 70mg of Erenumab every 28 days. Neurologists administrate MIDAS, HIT-6 and BDI and scales to study sleep impact of erenumab(MEQ-SA, PSQI, SCI, ESS), every month for first 3 months treatment, and then every 3 months.

Results:: We enrolled 88 patients: 38 migraineurs underwent to 140mg and remaining to 70mg. Erenumab reduce significantly monthly-migraine-days (MMD) from 1st month to 12-month treatment(Graph1,2), improving disability and depression(Graph3). Drug overuse is eliminated in 80% of patients as early as 3-month treatment. Dosage of 140mg is more effective than 70mg up to 6-month treatment in reduction of MMD(Graph2). At 3 month there is a reduction of the morning chronotype in favor of the intermediate one(Graph4) and in insomnia. Most common adverse event is constipation, which is observed in 9 patients(10%). No adverse events led to withdraw.

Graph 1: Decrease in MMDs compared to baseline
Graph 2. Responder 70mg vs 140mg
Conclusions:: Our real-life data confirm the efficacy and safety of erenumab in chronic migraine up to one year treatment with a significant improvement on quality of life. It is the first study that evaluate the effect of Erenumab on sleep: it could be attributed to an improvement in headache or to Erenumab action on CGRP, that is implicated in the mechanism underlying circadian rhythm.
ONABOTULINUMTOXINA REDUCE VISUAL CORTICAL EXCITABILITY IN CHRONIC MIGRAINE: PRELIMINARY RESULTS OF A STUDY WITH SOUND INDUCED FLASH ILLUSIONS

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Background and Aims:: The number of sound-induced flash illusions (SIFI) perceived are related with the level of visual cortex (V1) excitability. In episodic migraineurs, in response to visual-acoustic illusions, V1 is hyperexcitable. The injection of botulinum toxin type A was approved as a therapy for chronic migraine (CM). Recent studies have correlated the action of botulinum toxin with the release of CGRP and cortical excitability. We used SIFI to evaluate the V1 excitability in CM at baseline and 3 months after treatment with botulinum toxin

Methods:: 15 CM candidated to onabotulinumtoxinA therapy and 12 control subjects in the same age range. CM were examined interictally. Visual and sound stimuli are presented with different combinations: multiple flash trials where a single beep causes the perception of less flashes (fusion illusion) and trial where multiple beeps with single flash, induce perception of more flashes (fission illusion). Each combination was randomly presented 10 times. At the end of each presentation the subject had to indicate the number of the flashes seen

Results:: First rmANOVA showed that healthy controls refer a higher number of flashes compared to chronic migraineurs, while the second analysis did not show significant changes in such scores before and after 3 months from the treatment, but planned comparisons showed a significant augmentation of scores in 1 flash 4 beeps combination.

Conclusions:: Data obtained suggest that chronic migraineurs manifest less fission illusions than healthy controls, consistently with previous studies. Furthermore, onabotulinumtoxinA restores, though partially, fission illusions and, consecutively, normalizes visual cortical excitability.
Background and Aims:: Lockdown measures have been introduced worldwide to contain the transmission of COVID-19. Italians were forced to stay at home changing their life-style. The aim of this study was to evaluate if remote working (RW) during first COVID-19 lockdown in Italy influenced chronic migraine (CM).

Methods:: The study was based on an e-mail survey addressed to CM patients of our headache center. Every patient in the study continued migraine therapy as appropriate during lockdown. We collected information about RW and variations of: migraine attack frequency, attack duration, pain intensity, drug efficacy between the previous month and first Italian COVID 19 lockdown.

Results:: A total of 92 patients completed the survey. Twenty patients switched to RW. Migraine attack frequency was stable in 37, increased in 31 and reduced in 24; migraine attack duration was stable in 51, increased in 22, reduced in 19. Migraine pain was stable or reduced in 60 and increased in 32. Migraine drug efficacy was stable in 68, reduced in 16 and increased in 8. Remote working was significant associated with reduced migraine attack duration (p<0.009) and increased drug efficacy (p<0.012).

Conclusions:: RW in our patients was associated with reduced migraine attack duration and increased drug efficacy. No data are present in literature concerning this point and we hypothesize that this improvement could be attributed to the distance from workplace and its stressor, and the possibility to manage time in a different manner.
DIFFERENT PERSONALITY PROFILES IN PATIENTS WITH CHRONIC CLUSTER HEADACHE: A DATA-DRIVEN APPROACH

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Background and Aims:: Chronic Cluster headache (CH) patients are usually comorbid to mood spectrum disorders, psychopathological symptoms and personality disorders, but the role of psychopathological aspects is still insufficiently explored. Our aim is to verify, by a data driven approach, if CH patients may be classified on the basis of personality trait disorders.

Methods:: We applied hierarchical cluster analysis (HCA) to classify 60 patients suffering from CH, based on values of the clinical personality pattern scales of the Millon Clinical Multiaxial Inventory-III (MCMI-III). Subgroup comparison on demographical data (age, sex, education) and clinical features (laterality, MCMI-III clinical scores) where subsequently performed.

Results:: The outcome of HCA revealed the existence of 3 groups of patients with different personality traits. Two groups had unique patterns. Group 1 (n = 20) had distinctive avoidant, borderline and schizotypal personality traits. Group 2 (n = 15) scored high on the obsessive-compulsive and histrionic personality traits. Group 3 (n = 25) did not show relevant patterns. Clinically, Group 2 had lower education level and higher level of post-traumatic stress symptoms and dysthymia than the other groups. CH hemispheric lateralization differed between groups with predominant right hemispheric manifestations for the Group 1.

Conclusions:: Our data-driven approach revealed different personality profiles in chronic CH patients with specific psychopathological features. Our findings also provided evidence on the role of individual factors, including cognitive reserve levels, on clinical manifestations. This might help to identify the most appropriate therapeutic strategies and predict the evolution of the disease.
HEADACHE AND SLEEP-RELATED BREATHING DISORDERS AMONG PATIENTS WITH SCLEROSTEOISIS AND DISEASE CARRIERS

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Background and Aims: Headache and sleep-related breathing disorders among patients with sclerosteosis and disease carriers have been little studied. This study aimed to investigate the clinical characteristics and neuroimaging of a large Italian family affected by hyperostosis of the skull due to sclerosteosis.

Methods: Patients and gene carriers underwent careful neurological examination, cranial CT, brain MRI and MR-venography, CSF pressure monitoring and polysomnography to assess the presence of sleep apnea.

Results: In this Italian family with sclerosteosis, genetic tests detected the homozygous mutation p.Gln24X (c.70C>T) of the SOST gene in the proband, and a heterozygous mutation between 9 siblings. Severe hyperostosis of the skull caused chronic headache secondary to intracranial hypertension due to venous hypertension and obstructive sleep apnea syndrome in adult homozygotes. There was transosseous intracranial-extracranial occipital venous drainage which indicated a compensatory mechanism for intracranial venous hypertension, one of the causative factors of increased CSF pressure in sclerosteosis. While mild hyperostosis of the skull was associated with headache and snoring in heterozygotes.

Conclusions: Headache and sleep-related breathing disorders are common clinical manifestations among patients with sclerosteosis and disease carriers. Cerebral venous hypertension leading to intracranial hypertension and facial deformities are the causative factors of headache and sleep-related breathing disorders. These data suggest that venous stenting to accommodate cerebral venous drainage could be useful in the treatment of intracranial hypertension, and correction of facial deformities to relieve obstructive sleep apnea may play a role in the treatment of patients with sclerosteosis. The data highlight that it is reasonable to extend neurological evaluation and radiological study to gene carriers.
Background and Aims:: Compare maternal, fetal and infant outcomes among pregnant women with migraine exposed to galcanezumab to those exposed or not exposed to other migraine medications. There is a need to study utilization and safety of these medications before/during pregnancy since data on outcomes of pregnancies exposed to galcanezumab is limited.

Methods:: This multidrug pregnancy registry will enroll women with migraine exposed to galcanezumab up to 5 half-lives before/during pregnancy. Pregnant women with migraine (exposed or not exposed to other migraine medications) will be enrolled into comparator groups. Eligible women may enroll or be enrolled by their Health Care Provider by calling the phone number/visiting the website listed in the US Package Insert. Information on mother and fetus/infant (eg, demographics/medical history/exposures/outcomes) will be collected at multiple time points during pregnancy and to 1 year post delivery.

Results:: The primary outcome assessed in this pregnancy registry is major congenital malformations. Additional maternal, fetal and infant outcomes (to 1 year of age) will be evaluated.

Conclusions:: Real-world studies are needed to evaluate utilization and safety of new migraine medication exposures in pregnancy. This registry is part of a larger effort towards this goal. Sufficient enrollment of pregnant women will enable execution of two comparative safety studies using this registry.
BACKGROUND AND AIDS: Coronavirus Disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a contagious disease that causes the current pandemic. SARS-CoV-2 has been postulated to have a neuroinvasive potential. Headache as a very common non-respiratory symptom of COVID-19. The literature review is intended to explain about headache in patients with SARS-CoV-2 infection.

METHODS: The journals used in literature reviews obtained through databases include Google Scholar, PubMed, and Science Direct. The search found 26 articles from Google Scholar, 3 from PubMed, and 6 articles from Science Direct. Of all the articles, the selection was made based on the title and abstract, so that 35 articles were obtained. The literature used is not a thesis, dissertation, thesis, or other literature review. The articles used are only journals in full text. So that the number of articles used is 25 articles.

RESULTS: From the 25-literature reviewed, headache in COVID-19 patients appears in the prodromal phase and is followed by anosmia/hyposmia. Headache on COVID-19 patients in general were holocranial, hemicranial, or occipital, pressing, and worsens with physical activity or head movements. Pathogenesis of headache on COVID-19 patients still under debated. The mechanism of headache in SARS-CoV-2 is related to cytokine storm and cytokine release syndrome (CRS).

CONCLUSIONS: Headache is one of the most common neurological manifestations in patients infected with SARS-CoV-2. The characteristic of headache in patient COVID-19 is typically a headache of moderate to severe intensity with frontal predominance and oppressive quality.
FUNCTIONAL RESTORATION WITH REYVOW (FREE): A US-BASED CROSS-SECTIONAL SURVEY IN PATIENTS TAKING LASMIDITAN

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Background and Aims:: Assess respondents’ ability to return to their usual activities and level of impairment of those activities after migraine acute treatment with lasmiditan.

Methods:: A 15-min web-based survey was conducted on adult respondents who had enrolled in the US patient support program, redeemed a savings card, and treated at least 1 migraine attack with lasmiditan within the prior month. Symptoms/outcomes/ability to engage in various activities after recent lasmiditan-treated migraine attack were assessed using descriptive statistics.

Results:: 78 respondents completed the survey (mean age 48 years/93.6% female/16.9 mean headache days/month). Untreated/unsuccessfully treated migraine attacks prior to ever taking lasmiditan resulted in inability/severely impaired ability to perform various activities (Table). At the time of lasmiditan dosing (most recent attack), 49% had severe and 45% had moderate pain. By 2-hours post-dose, 94% respondents had some/complete pain improvement. After lasmiditan treatment, 45-75% respondents returned to their current/planned activities, except for planned activities outside home (22%). Extent of ability to perform current/planned activities varied by activity (Table). 77% respondents were satisfied with lasmiditan; 62% were satisfied with its ability to return them to their usual activities.
**Conclusions:** With lasmiditan, majority respondents were satisfied and able to return to their usual activities with no/some degree of impairment.

| Past impact of untreated or unsuccessfully treated migraine attack (prior to ever taking lasmiditan), n (N), % | Usual activities |
|---|---|---|---|---|---|
| | Interacting with family, friends, and others who are close to you | Performing leisure time activities | Dealing with household chores | Dealing with activities outside the home | Performing work or school tasks |
| Completely unable to perform activity | 28 (78), 36 | 37 (78), 47 | 32 (78), 41 | 41 (78), 53 | 33 (78), 42 |
| Activity severely impaired | 34 (78), 44 | 23 (78), 30 | 28 (78), 36 | 24 (78), 31 | 28 (78), 36 |
| Activity impaired to some degree | 14 (78), 18 | 14 (78), 18 | 16 (78), 21 | 12 (78), 15 | 8 (78), 10 |
| Activity not impaired | 1 (78), 1 | 2 (78), 3 | 0 (78), 0 | 0 (78), 0 | 0 (78), 0 |
| Not Applicable | 1 (78), 1 | 2 (78), 3 | 2 (78), 3 | 1 (78), 1 | 9 (78), 12 |

**Activity engaged in at the time of taking lasmiditan, n (N), %**

| Ability to return to activity (among those who performed this activity) | Usual activities |
|---|---|---|---|---|---|
| | Interacting with family, friends, and others who are close to you | Performing leisure time activities | Dealing with household chores | Dealing with activities outside the home | Performing work or school tasks |
| Severe | 8 (14), 57 | 9 (12), 75 | 12 (16), 75 | 6 (9), 67 | 19 (29), 65 |
| Impaired to some degree | 5 (8), 63 | 6 (9), 67 | 8 (12), 67 | 3 (6), 50 | 11 (19), 58 |
ONABOTULINUMTOXIN-A DURING COVID-19 PANDEMIC: LONG-TERM EFFICACY IN CHRONIC MIGRAINE.

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Background and Aims:: Current guidelines recommend regulare quarterly administration of Onabotulinumtoxin-A in chronic migraine patients. During the first Italian COVID-19 related quarantine period, as per national and international guidelines, Onabotulinumtoxin-A administrations were suspended, given its biological risk. Aim of the present study was to assess migraine outcome in patients in prophylaxis with Onabotulinumtoxin-A during COVID-19 related treatment suspension (March-May 2020).

Methods:: This is a retrospective observational study, conducted at the Headache Centre – ASST Spedali Civili Brescia. All patients scheduled for Onabotulinumtoxin-A treatment during March-May 2020, whose administration was suspended, were included.

Results:: Forty-two consecutive patients were enrolled. All patients had a diagnosis of chronic migraine and medication overuse. On average, patients were in their 4th treatment cycle (range 3-10), due to the COVID-19 treatment suspension, with a six months – instead of three – gap between administrations. Considering this cohort of patients, as of February 2020, 45.2% were non-responders, 19% were partial responders, and 35.7% were full responders. Post-COVID-19 suspension, up to 45.2% of patients were full responders and 26.2% partial-responders. Analysing single patients, seven patients remained non-responders and twelve remained full-responders, whereas nine worsened and fourteen improved compared to pre-COVID-19.

Conclusions:: Despite treatment delay, Onabotulinumtoxin-A still proved its efficacy in migraine prevention. The progressive increase in responders rates usually seen at subsequent treatments was still evident, regardless of the missing administration.
PROJECT FOR THE ESTABLISHMENT OF THE ITALIAN MIGRAINE REGISTRY (I-GRAINE-NEW)

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Background and Aims:: Migraine is the leading cause of disability in people under 50 but remains underdiagnosed and undertreated. A comprehensive appraisal of the full clinical, social and economic complexity of the disease is a fundamental prerequisite for its proper management. I-GRAINE-NEW aims to: provide information on migraine natural history, provide epidemiological, social and sanitary resource use data, identify the impact of patient management on prognosis.

Methods:: Data will be collected by 41 headache centers. I-GRAINE-NEW will enroll a representative sample of 10% of adult patients with migraine and will last at least 5 years. Patients will be evaluated by face-to-face interviews using a detailed semi-structured questionnaire. A subgroup of 6000 patients, referred for a first outpatient visit, will be considered for a retrospective-prospective sub-study.

Results:: I-GRAINE-NEW will include 10% of all the adult patients affected by episodic or chronic migraine visited at each center for at 5 years. Patients will be evaluated by face-to-face interviews using a detailed (~200 items), semi-structured questionnaire assessing socio-demographic factors, lifestyle, medical history, migraine characteristics and disability, patient’s journey and healthcare resource use. A subgroup of 6000 incident migraine patients referred for a first outpatient visit, will be considered for a retrospective-prospective cohort study - lasting 24 months - aimed of analysing more in-depth (~500 items questionnaire) clinical endophenotypes, treatments and the detailed history of migraine onset and evolution.

Conclusions:: The I-GRAINE registry is expected to shed light on migraine unmet needs, define the endophenotypes, and improve clinical management, resulting in increased disease awareness, better healthcare resource allocation, and reduced economic burden.
CGRP MONOCLONAL ANTIBODIES EARLY ONSET OF EFFICACY FOLLOWING FOUR WEEKS OF TREATMENT IN CHRONIC MIGRAINE

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Background and Aims:: Various studies have documented a rapid onset of efficacy in migraine prevention for monoclonal antibodies targeting CGRP. Aim of the present study was to assess migraine outcome following the first 4 weeks of treatment in patients treated with erenumab 70 mg or galcanezumab 240 mg (loading dose).

Methods:: This is a retrospective observational study, conducted at the Headache Centre – ASST Spedali Civili Brescia. All patients with a 4 weeks follow-up at March 2021 and a diagnosis of chronic migraine were included.

Results:: Seventy-four consecutive patients were enrolled, of whom 50 in treatment with erenumab and 24 with galcanezumab. All patients had a diagnosis of chronic migraine, of whom 64 also documented medication overuse. Following the first administration, a significant reduction in terms of migraine days (11.3±0.7 vs 20.9±0.9; p < 0.001), analgesics consumption (11.7±1.2 vs 24.1±1.9; p < 0.001) and pain intensity (6.3±0.2 vs 7.6±0.1; p < 0.001) compared to baseline, was found. At week 4, 58.9% of patient documented an overall significant clinical response (lost >50% migraine days compared to baseline). No significant differences were found between erenumab and galcanezumab both at baseline and week 4.

Conclusions:: The present study confirms monoclonal antibodies targeting CGRP rapid onset of efficacy, as early as from the very first administration, regardless of the type of monoclonal antibody.
FREMANEZUMAB IN THE PREVENTION OF HIGH-FREQUENCY EPISODIC AND CHRONIC MIGRAINE: FRIEND (FREMANEZUMAB IN REAL WORLD STUDY), THE FIRST ITALIAN MULTICENTER, PROSPECTIVE REAL-LIFE STUDY.

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Background and Aims:: We assessed fremanezumab effectiveness, safety and tolerability in high-frequency EM (HFEM) and CM in a real-life population.

Methods:: This is a 24-week, multicenter (n=9), longitudinal, cohort, real life study performed from 28/01/2020 to 15/03/2021. We considered all consecutive patients with HFEM or CM aged 18-65 years. Change in monthly migraine days (MMD) at weeks 21-24 compared to baseline was the primary efficacy endpoint. Secondary endpoints encompassed variation in monthly analgesic intake and change in VAS, HIT-6 and MIDAS scores during the same time interval.

Results:: 47 patients received >1 fremanezumab dose (225 mg monthly, n=38; 625 mg quarterly, n=9). Thirty-one patients were treated for 24 weeks and considered for effectiveness analysis. From baseline to weeks 21-24, fremanezumab treatment induced a significant reduction in MMD (-8.9±5.3,p<0.001), analgesic intake (-12.7±9.8,p<0.001), and VAS (-3.0±2.6,p<0.001), HIT-6 (-13.8±9.5,p<0.001) and MIDAS scores (-69.7±57.5,p<0.001). 4 patients (8.5%) presented adverse events: injection site erythema (2), orticaroid reaction (2), abdominal colic (1). Only 1 patient discontinued for ineffectiveness.

Conclusions:: 24-week fremanezumab treatment provides effectiveness, safety and tolerability in real-life patients with HFEM or CM with >3 prior preventive treatment failures. Our data need to be confirmed in larger studies.
Background and Aims:: Recent studies have showed that in emergency department (ED) pediatric admissions for headache are increasing in the last years. However Covid-19 pandemic may have changed the use of health services for several reasons. Aim of this study is to analyze the rates of admission for pediatric headaches in ED before and during Covid-19 Pandemic.

Methods:: we have collected retrospectively the records of children (range of age 5-14) admitted on ED in 2012, 2019 and 2020. We selected the records including Headache and Headache associated to other symptoms (vomit, fever, dizziness, etc.), collecting further the use of computed tomography (CT) and neurological consultation.

Results:: In 2012, 2019 and 2020 the cephalaligic children admitted to ED were respectively 313/18806 (1.66%), 407/15605 (2.61%) and 234/9630 (2.43%). The admission rates for headaches shows highly significant differences between 2012 and biennial 2019/2020. There are no differences in use of CT and neurological consultations. The only difference in access was the initial drop in the first months of lockdown (2020/80% vs 2019/50%).

Conclusions:: Our data support the increase of admission for headache to the pediatric ED in the last ten years. However the Covid-19 pandemic has not increased the admission rate compared to 2019 neither the use of CT or neurological consultations. The fear of using EDs was no changed for headache compared to other pediatric alarm symptoms.
COST-EFFECTIVENESS ANALYSIS FOR PRIMARY HEADACHE IN SAMPLE SIZE, MONGOLIA

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Background and Aims:: Headache disorders are most prevalent public-health problem, affecting people in all countries. GBD2016 and GBD2017 established their high ranking among all causes of years lived with disability (YLDs). Evidence of the cost and effects of interventions for reducing the global burden of headache, usually chronic headache and migraine.

Methods:: In simple size, inpatient and outpatient headache suffers aged 18-65 were selected on ICHD-3. We assessed Headache-Attributed Lost Time (HALT) questionnaire. Individual and population-level disability attributed to migraine, TTH and chronic headache using disability weights (DWs) from GBD2017 for the ictal states of each. Enquire Indirect cost per patient and cost of Temporary loss of work ability

Results:: Disability level, estimated by applying the GBD2017 DW for the ictal state of migraine was 5.5%, chronic headache was 14.6% higher than TTH was 0.17%. People with headache on ≥15 days/month had markedly and significantly lower incomes than those headache on ≤15 days/month (p=0.004) HALT scores were higher in people with migraine than tension type headache (p=0.001). The average annual indirect cost per patient was USD4789, cost of temporary loss of work ability was USD2357.

Conclusions:: Headache disorders are not only common in Mongolia but also heavily burdensome, with a very similar picture to Nepal, Ethiopia and Russia. Individual disabilities attributable to all headache types make up a total disability of 1.7% among the entire population aged 18-65 years. It is important to recognize that this population is effectively the working population. This is enormous economic burden in a lower-middle-income country, likely to be reflected in national and gross domestic product.
HEADACHES AND SLEEP PROBLEMS AMONG THE MEDICAL STAFF

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Background and Aims:: This study was aimed to investigate the associations of sleep quality, symptoms and disorders with specific headache subtypes among the Mongolian medical staff.

Methods:: This cross-sectional survey consisting of semi-structured questionnaires was administered to 290 participants of medical staff from randomly selected state hospitals during the period from September to October 2019 in Ulaanbaatar, Mongolia. We used the Pittsburgh Sleep Quality Index (PSQI) and questionnaire of primary headache was based on the criteria of the International Classification of Headache Disorders-III.

Results:: We surveyed totally 290 participants; of them, 243 (83.8%) were females and 47 (16.2%) were males. The one-year prevalence of all types of headache was 235 (81.0%). The prevalence of migraine and tension-type headache was 36 (12.4%) and 43 (14.8%), respectively. Poor sleep quality was present in 187 (64.5%) of participants associated with sleep time (p=0.003), wake-up time (p=0.001), sleep latency (p<0.001), total hours slept (p<0.001), subjective sleep quality (p<0.001) and 1-year all headaches (p<0.001). There was no significant difference in sleep quality between participants with and without migraine or tension type headache. However, staff with 1-year all headaches reported significantly higher mean score of PSQI (p<0.001), less sleep duration (p=0.008), lower subjective sleep quality (p<0.001), higher day time sleepiness (p=0.032) and poor day time execution (p=0.018) than those without headache.

Conclusions:: Our study findings reveal that poor sleep quality and headaches are highly prevalent among the Mongolian medical staff. The short sleep duration and poor sleep quality index are associated with an increased 1-year headache symptoms.
CACNA1A-P.THR501MET MUTATION ASSOCIATED WITH FAMILIAL HEMIPLEGIC MIGRAINE: A FAMILY REPORT.

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Background and Aims:: Hemiplegic migraine (HM) is a rare form of migraine characterized by the presence of motor and other types of aura. HM can be sporadic or familial. Familial hemiplegic migraine (FHM) is an autosomal dominant disorder, classified into 3 subtypes, based on the gene involved (CACNA1A in FHM1, ATP1A2 in FHM2 and SCN1A in FHM3). The clinical presentation is highly heterogeneous and some attacks may be severe. We report the clinical characteristics and genetic analysis of 12 patients belonging to a family with CACNA1A-p.Thr501Met gene mutation.

Methods:: We screened for mutations in CACNA1A gene 15 subjects belonging to the same family (Figure 1). The exonic sequences of CACNA1A were analyzed using a Tru-seq® Custom Amplicon (TSCA) (Illumina Inc., San Diego, CA) targeted capture and paired end library kit. Sanger sequencing was used to confirm CACNA1A variants and segregation analysis.

Results:: CACNA1A-p.Thr501Met mutation was found in 12 of the 15 patients screened, compatible with the diagnosis of FHM1 (Table 1). Attacks of HM² were reported by 10 of the 12 subjects (83.33%). Only one subject developed persistent cerebellar symptoms and none of the subjects developed cerebellar atrophy.
Conclusions:: The variant p.Thr501Met was described previously in association with episodic ataxia and rarely with FHM related to cerebellar symptoms. FHM1 has a broad clinical spectrum and about half of the families have cerebellar involvement. In our study, only one patient developed persistent cerebellar deficits. These data suggest that CACNA1A-p.Thr501Met mutation can occur prevalently as hemiplegic migraine.
CAN HEADACHE BE CONSIDERED AN ALTERED FUNCTION OF ATTENTIVE PROCESS?

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Background and Aims:: In this study we want to analyse the role played by cognitive evoked potentials in individuals suffering from headache vs. non-cephalalgic subjects. Using as differential variables the amplitude and latency values of the visual and auditory P300 recorded in the FZ CZ PZ derivations,

Methods:: All enrolled subjects arrived at my outclinic for a neurological evaluation and as usual they underwent a series of evaluations to highlight whether the headache was attributable to some organic factor. 44 subjects with headache: 10 males and 34 females aged 18 to 65 years. The control group had no history of headache, 13 subjects: 4 males and 9 females. All subjects were subjected to a preliminary EEG with open eyes and closed eyes to highlight the presence of irritative phenomena. Registration of ERP, the paradigm used is ODDBALL.

Results:: The values of the amplitudes in the FZ CZ PZ derivations of the controls vs. headache group it is evident that in all 3 derivations the difference in amplitude is significantly different between normal and headache both for the visual P300 and for the auditory P300.

Conclusions:: The results obtained from this study, say that attention deficit is present in the subjects affected by headache and that could influence in a statistically significant matter their schooling and as a consequence their quality of life as well. Thus, the subjects with an attention deficit will have a bigger difficulty both in the performance and in the learning process too. This predisposes to anxiety disorders, depression.
Background and Aims:: Headache is the most common presentation in neurology and role of transcranial doppler (TCD) in headache disorders specially migraine and Idiopathic intracranial hypertension (IIH) has not been explored in the past. The present study was planned to decipher the role of TCD to assess the status of flow dynamics in the vessels, which may help in deciding appropriate therapeutic options in headache disorders.

Methods:: This prospective study was carried out at a tertiary care institute in North India and included 51 people with IIH (fulfilling Modified dandy criteria), 87 with migraine (diagnosed as per ICHD 3), and 101 healthy controls. All patients and controls were subjected for transcranial doppler study including vasomotor reactivity.

Results:: Mean age of patients in IIH was 33.41 years, in migraine was 34.6 years and in control group was 31.17 years. Vision loss was present in 66.67% patients of IIH. Neuroimaging was abnormal in 94.11% patients of IIH with mean CSF pressure of 31.27±5.32 cm. Mean VMR in IIH (1.11±0.32) was lower than mean VMR in migraine (1.34±0.43) and controls (1.49±0.46%) suggesting different pathophysiological mechanisms in them. Statistically significant difference between MCA mean flow velocity (MFV) and end diastolic velocity (EDV) was present when compared between IIH, migraine and controls. With increasing CSF pressure, pulsatility index showed a positive correlation (p value=0.045).

Conclusions:: TCD derived MCA flow velocities and indices differ considerably between IIH, migraine and controls and may be utilized in these patients to explain the pathogenetic mechanisms and clinical picture. More-over pulsatility index may be useful for non-invasive monitoring of raised ICP.
EFFECTS OF COVID-19 ON A MIGRAINOUS PATIENT TREATED WITH ERENUMAB: A CASE REPORT

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Background and Aims:: Headache is a frequent symptom of the novel coronavirus 19 disease (COVID-19). Two distinct headache phenotypes were observed in COVID-19 patients: one showing the features of migraine attacks while another characterized by symptoms of tension-type headache. We report the effects of SARS-CoV-2 infection on a chronic migraine patient treated with erenumab.

Methods:: A 47 years old patient suffering of chronic migraine started, in September 2020, an anti-CGRP receptor monoclonal antibody therapy with Erenumab, at the dosage of 70 mg per month. In a two-months period, headache frequency decreased from 16 to 5 attacks per month. On the third month the patient developed mild COVID-19 symptoms, like fatigue and hyposmia, with nasopharingeal swab-test resulting positive for SARS-CoV-2 RNA. A significant increase in migraine attacks (15 per months) was reported. Brain MRI and EEG were performed, resulting normal. Erenumab was increased to 140 mg/month.

Results:: After increase in anti-CGRP dosage, the frequency of migraine attacks progressively decreased to 3-4 per month and remained stable. All the headaches experienced by our patient during the infection fulfilled the criteria of the migraine attacks, without tensive like features.

Conclusions:: Our case report suggests that inflammatory processes induced by SARS-CoV-2 infection may increase the frequency of migraine attacks through an activation of the trigeminovascular system. Additional studies with anti-CGRP monoclonal antibodies in COVID-19 patients are needed.
TRANSCRANIAL DOPPLER ULTRASONOGRAPHY STUDY IN MIGRAINE PATIENTS TREATED WITH ERENUMAB

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Background and Aims:: Pathogenesis of migraine is believed to be neurogenic, with vascular changes having a role in the attack pathophysiology. Migraine patients have reported abnormalities in cerebral hemodynamics. Human monoclonal antibodies represent the new therapy of migraine, acting against the vasodilator effect of Calcitonin gene-related peptide. In this frame, the aim of the present study was to evaluate blood flow velocities in basal brain arteries and vasomotor reactivity of migraine patients using TCCD, before and after monoclonal antibody treatment with erenumab.

Methods:: 11 patients with migraine without aura treated with erenumab were age-matched with 11 healthy controls. Peak Systolic Blood Flow Velocity (PSV), End-Diastolic Blood Flow Velocity (EDV), Mean Blood Flow Velocity (MBFV), Pulsatility Index (PI), and Resistivity Index (RI) were recorded from the Middle Cerebral Artery (MCA) bilaterally and Basilar Artery (BA). Cerebrovascular reactivity to breath-holding was also evaluated. Patients were evaluated at baseline, after 6 months from the first erenumab injection and after one year of treatment.

Results:: A significant difference was observed in MBFV and PSV of the MCA in patients after one year of treatment with erenumab. In particular, patients exhibited a decrease in MBFV (p=0.009) and PSV (p=0.020) compared to controls.

Conclusions:: Cerebral hemodynamics are partially changed in migraine patients after a long period of treatment with erenumab.
RETROSPECTIVE ANALYSIS OF ADULT CHRONIC POST-TRAUMATIC HEADACHE WITH RESPECT TO THE INTRACRANIAL PRESSURE AND THE CHARACTERISTIC OF HEADACHE

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Background and Aims:: Chronic post-traumatic headache (CPTH) is a life disturbing disorder with many symptoms (JAMA 2008; 300: 71-9) and yet the characteristic of the headache is still unclear. We have reported the possibility of increased intracranial pressure (ICP) in adult CPTH (Eur J Med Res 2007; 12: 246-54)). The main purpose of this study is to elucidate the intracranial pressure (ICP) and the characteristic of the headache.

Methods:: We retrospectively investigated 150 adult patients (≥20 years) with CPTH over 3 months. ICP was measured by lumbar spinal tap in all patients. Data were shown in mean (SD). Statistically significant level was set p<0.05.

Results:: Mean age was 42.1 (13.5) years (40.7 (11.1) years for male (n=58) and 43.0 (14.8) years for female (n=92), p=0.318). Mean ICP was 151.2(44.9) mmH₂O (167.1 (44.5) mmH₂O for male and 141.2 (42.6) mmH₂O for female p<0.001). Disease period was 68.1 (101) months. One hundred and thirty-two patients had headache with orthostatic nature and 116 patients complained deterioration of the headache by low atmospheric pressure. Thirty-one patients complained whole body pain similar to fibromyalgia. Removal of cerebrospinal fluid (CSF) was effective to relieve symptoms in 77 patients.

Conclusions:: Although many patients with CPTH complained headache with orthostatic nature suggesting low ICP, their ICP was normal or even high. Female ICP was significantly lower than male ICP. CSF removal was effective in many patients. The results of this study indicates the involvement of CSF abnormality in CPTH.
Background and Aims:: Neurocysticercosis is an infection caused by the larval stage of the tapeworm Taenia solium. The clinical manifestations depend on load, type, size, location, stage of development of the cysticerci, and the host's immune response against the parasite. An intraventricular cysticercus can produce Bruns syndrome, which can manifest as a thunderclap headache. Here we present an unusual case.

Methods:: The methodology is a case report.

Results:: 27-year-old male, industrial technician, from Barranquilla, Colombia, with no relevant pathological history. The patient pick up an object on the floor, tilting his head, later when changing from crouched to standing position, he triggered a thunderclap headache, followed by multiple emetic episodes and a feeling of dizziness. The intensity of the pain decreased during the following hours, yet returning or increasing when tilting the head. The biomarkers were within normal range, the cranial computed tomography evidenced multiple cortical calcifications, triventricular hydrocephalus without signs of activity (figure 1). The contrast cerebral magnetic resonance found a cystic mass in the third ventricle with a scolex, which corresponds to the vesicular phase of the cysticercus (figure 2). The patient received endoscopic surgical management with subsequent improvement. Figure 1.
Conclusions: The syndrome was first described in 1902 by Lugwig Bruns. Characterized by attacks of sudden severe headache, vomiting, and vertigo precipitated due to abrupt movements of the head due to presence of mobile deformable intraventricular lesion. Due to intermittent or positional obstruction resulting from ball-valve mechanism, causing episodic obstructive hydrocephalus. This case supports that neurocysticercosis can cause thunderclap headache.
CHRONIC MIGRAINE WITH MEDICATION OVERUSE HEADACHE: IS DETOXIFICATION STILL NECESSARY IN THE ERA OF NEW PROPHYLAXES?

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Background and Aims:: Medication overuse headache (MOH) leads to high disability and poor quality of life; the debate on value and method of detoxification is still open, even more at the present time with new preventive treatments available. The aim of this study is to estimate the effectiveness of detoxification in multi-resistant chronic migraine (CM) with MOH patients who start prophylaxes Anti-CGRP monoclonal antibodies (mAb).

Methods:: Prospective analysis of all CM with MOH patients with at least 28 monthly headache days (MHD) who started a prophylaxis with Anti-CGRP, with or without detoxification at the beginning of treatment, at Bologna Headache Center between June 2019 and December 2020. We evaluated CM remission and MHD reduction (>50% response) at three months.

Results:: 39 patients were included; 26 started prophylaxis alone (PA), 13 started prophylaxis after detoxification (PAD). At 3-months we observed clinical conversion to episodic migraine in five of the 26 PA patients (19.2%) and in five (38.4%) (p 0.1) of the 13 PAD group. Mean MHD was 22.2 (± 8.1) in the PA group and 16.3 (± 10.2) in the PAD group (p 0.11); >50% responders were five of the 13 PAD patients (38.4%) and four of the 26 PA patients (19.2%) (p 0.1).

Conclusions:: Detoxification seems to maintain a key role in preventive treatment of CM with MOH patients, also in the era of new prophylaxes. Larger samples are warranted to obtain definitive results.
EVALUATION OF PREVALENCE AND SEVERITY OF OBSTRUCTIVE SLEEP APNEA USING OVERNIGHT - POLYSOMNOGRAPHY IN PATIENTS WITH IDIOPATHIC INTRACRANIAL HYPERTENSION

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Background and Aims:: Background: Patients with idiopathic intracranial hypertension (IIH) frequently have co-existent obstructive sleep apnea (OSA). It has been postulated that OSA, which causes apnea and hypopnea might be a contributing factor for the increased intracranial pressure, thereby contributing to IIH. We aimed to assess the prevalence of OSA among patients of IIH and evaluate its influence on the severity of IIH. Aims: To assess the prevalence of obstructive sleep apnea (OSA) among patients of Idiopathic Intracranial hypertension using overnight polysomnography (PSG) and evaluate its influence on the severity of IIH.

Methods:: In this case-control study, 18 cases of IIH and 12 controls were enrolled. Baseline clinical characteristics were noted. Assessment of different sleep abnormalities was done with different questionnaires e.g Berlin questionnaire for OSA, Pittsburgh Sleep Quality Index (PSQI) for overall sleep quality, Insomnia Severity Index (ISI) for Insomnia and RLS rating scale and PSG.

Results:: The mean age of IIH patients was 36.2 ± 10.9 years. 94.4% were female. The mean CSF pressure of cases was 33.25 ± 5.8mm H2O. A high risk of OSA was observed in 55.5% of cases and 33.3% of controls. Overnight PSG was conducted on 12 cases and 6 controls. 50% of cases had no OSA, 33.3% mild OSA, and 16.6% moderate OSA in comparison to 66.6%, 33.3%, and 0% in the control arm. IIH patients had poorer sleep quality (PSQI>5) and more RLS score in comparison to healthy controls.

Conclusions:: There was a higher prevalence of OSA in patients with IIH in comparison to healthy controls.
FEATURES OF A HEADACHE AFTER COVID-19 IN PATIENTS WITH PRIMARY HEADACHES

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Background and Aims:: The COVID-19 pandemic had a general adverse effect on patients with primary headaches. Both the COVID-19 and the psycho-emotional and social factors that accompany the pandemic affected the characteristics and course of primary headaches in many patients.

Methods:: Analysis of clinical cases of 38 patients with post-COVID syndrome and primary headache in anamnesis who were examined and treated by neurologists at the Delta Med medical center in 2020-2021.

Results:: During the acute phase of COVID-19, among the examined patients, 27 had a headache which was different from regular. 15 patients had a history of migraine, 23 had a history of tension-type headache before COVID-19. After COVID-19 most of the patients with migraine noted more frequent and intense attacks, 2 developed status migrainosus, in 46.7% of patients migraine transformed into chronic. Patients with TTH in most of the cases also noted an increase in both frequency and intensity of headache, but in addition, in some patients the headache pattern changed, there were signs of neuropathic component of pain, confirmed by Pain Detect. More frequent attacks led to excessive drug use. Out of 38 patients, 7(18.42%) were diagnosed with medication overuse headache in the structure of the post-COVID syndrome. 5 patients with migraine had small foci of gliosis on MRI.

Conclusions:: Most patients experience an increase in the frequency and severity of headache after COVID-19, and some patients show signs of neuropathic pain. Some of the patients engaged in self-medication and abused analgesics, which in combination with treatment of COVID-19 led to medication overuse headache.
FREMANEZUMAB IMPROVES QUALITY OF LIFE IN PATIENTS WITH HIGH- AND MODERATE-FREQUENCY EPISODIC MIGRAINE

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Background and Aims:: Patients with migraine may experience increasing disease burden as migraine frequency increases. This pooled analysis evaluated quality-of-life and disability outcomes with fremanezumab, a fully-humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), in patients with high-frequency episodic migraine (HFEM; 10-14 days/month) or moderate-frequency episodic migraine (MFEM; 4-9 days/month) from 2 double-blind phase 3 studies (HALO EM and FOCUS).

Methods:: In HALO EM and FOCUS (patients with inadequate response to 2-4 prior preventive treatment classes), patients were randomized 1:1:1 to quarterly fremanezumab, monthly fremanezumab, or placebo. Changes from baseline in Migraine-Specific Quality of Life (MSQoL) and Migraine Disability Assessment (MIDAS) scores were assessed in HFEM and MFEM subgroups during the 4 weeks after third study drug dose.

Results:: Analyses included 659 patients with MFEM and 515 with HFEM. Least-squares mean changes from baseline in MSQoL role-function restrictive scores were significantly greater with both fremanezumab dosing regimens versus placebo in MFEM (quarterly, 20.6; monthly, 21.7; placebo, 13.7; P<0.0001) and HFEM (quarterly, 17.2; monthly, 21.4; placebo, 13.1; P≤0.0343) subgroups, as were changes in role-function preventive (RFP) and emotional function (EF) scores for MFEM subgroup (both regimens; P≤0.0009) and changes in RFP (monthly dosing; P=0.0002) and EF scores (both regimens; P≤0.0498) for HFEM subgroup. Reductions from baseline in MIDAS scores were also greater with fremanezumab versus placebo (MFEM: quarterly, −23.5; monthly, −23.2; placebo, −16.0; P<0.0001; HFEM: quarterly, −23.3; monthly, −27.9; placebo, −16.7; P≤0.0150).

Conclusions:: Quality-of-life and disability were improved with fremanezumab versus placebo in patients with MFEM or HFEM.
LONG-TERM (>48 WEEKS) SAFETY AND TOLERABILITY OF ERENUMAB IN REAL-LIFE.

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Background and Aims:: Background: Erenumab proved to be safe and well tolerated in a 5-year continuation of a 1-year double-blind, placebo-controlled study. Aim: to assess >48-week erenumab tolerability and safety in a real-world setting.

Methods:: In this long term (>48-week), multicenter (n=15), longitudinal cohort real life study, we monitored all the adverse events emerged in consecutive adult patients with high-frequency episodic migraine (HFEM) or chronic migraine (CM) treated with monthly erenumab 70 mg or 140 mg from 20 December 2018 to 15 December 2020.

Results:: 442 patients (HFEM: 115; CM: 327) were treated with erenumab for >48 weeks: 209 (47.3%) patients were treated for 49-60 weeks, 132 (29.9%) for 61-72 weeks; 73 (16.5%) for 73-84 weeks; 21 (4.7%) for 85-100 weeks. Overall, >1 treatment emergent adverse event (TEAE) was reported by 136 (30.8%) [HFEM: 43 (37.4%); CM: 93 (28.4%)]. Most common TEAE were constipation (n =66; 14.9 %), injection site erythema (n =15; 3.4%), and influenza (n =7; 1.6%). Serious adverse events (SAE) were reported by 8 patients (1.8%) and led to treatment discontinuation: severe constipation (n=3), abdominal pain (n=1), NSTEMI (n=3), Covid-19 infection (n=1). Only severe constipation was considered treatment-related SAE (0.45%).

Conclusions:: Conclusion: Erenumab is safe and well tolerated also in long-term treatment (>48 weeks) in real life.
THE RARE COEXISTENCE OF TRIGEMINAL AUTONOMIC CEPHALALGIA (TAC) WITH TRIGEMINAL NEURALGIA (TIC DOLOROUX) IN THE SAME PATIENT: TAC-TIC HEADACHES - A CASE SERIES

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Background and Aims:: The occurrence of Trigeminal Neuralgia, also known as tic-doloroux (Tic), and TAC headaches ipsilaterally in the same patient is rare. We describe a series of Sri Lankan patients with TAC-tics with an emphasis on clinical significance, pathophysiological conjectures and a literature review.

Methods:: Four patients having TAC-tic combination were evaluated using clinical history and brain MRI.

Results:: Two males had CH-tic and CPH-tic respectively whilst one female had CPH-tic & the other had probable CPH-tic. Male with CPH-tic initially had Tics involving all 3 branches of trigeminal nerve, followed by CPH 5 months later, whereas other 3 patients developed V1 Tics and TAC headaches simultaneously. CH-tic patient had Tics for about 3 days prior to a bout of CH, around the same time of the day as CH attacks, while others had both types of headaches occurring simultaneously as well as separately. MRI brain with CISS sequence demonstrated stretching of ipsilateral trigeminal nerve by vascular loops in all except CH-tic patient, who had a vascular loop near the trigeminal nerve without impingement. All patients had satisfactory response to combination treatment targeting both TACs and Tics.

Conclusions:: Strictly unilateral nature, overlapping clinical features, the combination of ipsilateral TACs and Tics in the same patient and the finding of trigeminal neuro-vascular conflict in our patients as well as in the available literature raises the possibility of a common structural aetiology for TACs and Tics. Further studies involving TACs, Tics and TAC-tic combinations with dedicated trigeminal nerve imaging would be beneficial to further evaluate this phenomenon.
SYMPTOMATIC CLUSTER-TIC SYNDROME DUE TO A MENINGIOMA

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Background and Aims:: The combination of TAC headaches with trigeminal neuralgia (tic-doloroux) is a rare occurrence. Several cases have been reported, including from Sri Lanka. Some were symptomatic TAC-tics, whilst a definite cause was not identified in others.

Methods:: We report a case of a Sri Lankan female with cluster-tic attacks, occurring symptomatically due to a meningioma.

Results:: A 52-year-old female presented with right side-locked headaches for 6 years. She had 1-2 very severe attacks lasting about 20 minutes every day, associated with agitation and ipsilateral cranial autonomic symptoms. Acute attacks showed significant improvement with high-flow oxygen. She developed comparatively less severe, brief, shock-like, stabbing pain in the right periorbital region 8 months prior to presentation, occurring in bouts lasting about 15 minutes a day, without autonomic symptoms or cutaneous triggers. Two types of pains occurred simultaneously as well as sequentially. Different combinations of preventive medication failed to reduce the frequency of both types of attacks. Brain MRI with gadolinium enhancement showed a meningioma along the lateral wall of cavernous sinus with impingement of right trigeminal nerve. Patient underwent surgical excision of the meningioma, with significant improvement of symptoms.

Conclusions:: This patient had features of chronic cluster headache and right-sided probable trigeminal neuralgia, attributable to the meningioma. Available literature has descriptions of many cases with this combination, and some of these were due to structural causes such as pituitary adenoma, demyelination plaques, arachnoid cysts and vascular loops. An extensive search for an underlying structural lesion should be done in all patients with TAC-Tics and isolated TACs.
EFFICACY AND IMPROVEMENTS IN DISABILITY AND QUALITY-OF-LIFE WITH FREMANEZUMAB OVER 6 MONTHS IN MIGRAINE PATIENTS WITH INADEQUATE RESPONSE BY MULTIPLE PRIOR PREVENTIVE TREATMENT CLASSES

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Background and Aims:: Fremanezumab, a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has demonstrated efficacy in patients with chronic and episodic migraine (CM and EM) and documented prior inadequate response by 2-4 classes of migraine preventive medication in the 12-week randomized, double-blind (DB), placebo-controlled period (DBP) of the phase 3b FOCUS study. Efficacy, disability, and health-related quality of life (HRQoL) were evaluated during the DBP and subsequent 12-week open-label extension (OLE) in patients reverting from CM (≥15 headache days [HD] before DBP) to EM (<15 HD at Months 1, 2, and 3 [DBP] or Months 4, 5, and 6 [OLE]).

Methods:: During the DBP, patients were randomized (1:1:1) to quarterly fremanezumab, monthly fremanezumab, or placebo. Patients completing the DBP entered the OLE, and all patients received 3 monthly doses of fremanezumab. Outcomes are summarized by DB randomization group.

Results:: Overall, 136 patients reverted from CM at baseline to EM during the DBP; 206 patients reverted during the OLE. Reductions from baseline in monthly migraine days, monthly headache days, and disability scores (6-item Headache Impact Test and Migraine Disability Assessment) achieved during the DBP were generally maintained or increased during the OLE, as were improvements in HRQoL, based on Migraine-specific Quality of Life domain scores (Table).

Conclusions:: Migraine patients with inadequate response by multiple prior migraine preventive medication classes who reverted from CM to EM achieved sustained, clinically meaningful reductions in migraine and headache days and improvements in disability and HRQoL over 6
Table. Efficacy, Disability, and HRQoL Outcomes in Patients Reverting from CM to EM

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Placebo (n=18)</th>
<th>Quarterly fremanezumab (n=59)</th>
<th>Monthly fremanezumab (n=59)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DBP</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMMD, mean (SD) change from BL during 12-week DBP</td>
<td>-5.6 (4.40)</td>
<td>-7.8 (3.71)</td>
<td>-8.6 (3.60)</td>
</tr>
<tr>
<td>MHD, mean (SD) change from BL during 12-week DBP</td>
<td>-4.7 (3.51)</td>
<td>-7.5 (3.79)</td>
<td>-8.4 (3.68)</td>
</tr>
<tr>
<td>HIT-6, mean (SD) change from BL to end of DBP</td>
<td>-4.4 (5.61)</td>
<td>-7.7 (6.53)</td>
<td>-9.6 (6.91)</td>
</tr>
<tr>
<td>MIDAS, mean (SD) change from BL to end of DBP</td>
<td>-28.1 (43.71)</td>
<td>-28.4 (39.01)</td>
<td>-42.9 (39.36)</td>
</tr>
<tr>
<td>MSQoL RFR, mean (SD) change from BL to end of DBP</td>
<td>13.7 (14.91)</td>
<td>22.7 (19.57)</td>
<td>27.9 (17.71)</td>
</tr>
<tr>
<td>MSQoL RFP, mean (SD) change from BL to end of DBP</td>
<td>12.2 (17.42)</td>
<td>15.5 (18.26)</td>
<td>24.0 (18.07)</td>
</tr>
<tr>
<td>MSQoL EF, mean (SD) change from BL to end of DBP</td>
<td>11.9 (15.26)</td>
<td>22.9 (27.30)</td>
<td>25.2 (22.04)</td>
</tr>
<tr>
<td><strong>OLE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMMD, mean (SD) change from BL during 12-week OLE</td>
<td>-9.3 (5.38)</td>
<td>-8.4 (3.87)</td>
<td>-9.0 (4.00)</td>
</tr>
<tr>
<td>MHD, mean (SD) change from BL during 12-week OLE</td>
<td>-8.4 (4.83)</td>
<td>-7.6 (4.22)</td>
<td>-8.7 (3.97)</td>
</tr>
<tr>
<td>HIT-6, mean (SD) change from BL to end of OLE</td>
<td>-10.4 (8.88)</td>
<td>-9.9 (6.69)</td>
<td>-10.5 (6.34)</td>
</tr>
<tr>
<td>MIDAS, mean (SD) change from BL to end of OLE</td>
<td>-41.0 (51.53)</td>
<td>-38.8 (41.79)</td>
<td>-52.7 (49.91)</td>
</tr>
<tr>
<td>MSQoL RFR, mean (SD) change from BL to end of OLE</td>
<td>25.6 (21.37)</td>
<td>29.9 (18.78)</td>
<td>30.7 (20.10)</td>
</tr>
<tr>
<td>MSQoL RFP, mean (SD) change from BL to EOT</td>
<td>19.9 (21.26)</td>
<td>24.0 (19.23)</td>
<td>26.3 (20.00)</td>
</tr>
<tr>
<td>MSQoL EF, mean (SD) change from BL to EOT</td>
<td>20.0 (23.76)</td>
<td>28.7 (23.81)</td>
<td>27.4 (23.95)</td>
</tr>
</tbody>
</table>

CM, chronic migraine; EM, episodic migraine; DBP, double-blind period; BL, baseline; MMMD, monthly migraine days; SD, standard deviation; MHD, monthly headache days; HIT-6, 6-item Headache Impact Test; MIDAS, Migraine Disability Assessment, MSQoL, Migraine-specific Quality of Life questionnaire; RFR, role functional-restrictive; RFP, role functional-preventive; EF, emotional function; OLE, open-label extension.
HEADACHE IN PATIENTS WITH COVID-19

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Background and Aims: Aims: To study cephalic manifestations in individuals who have undergone COVID-19 to determine the frequency of occurrence and to assess the relationship of cephalgia with a new coronavirus infection.

Methods: There was developed a questionnaire that included points about the characteristics of cephalgia in this disease. Possible changes in the picture of headache during the pandemic, in people suffering from it earlier, were studied, as well as the characteristics of the newly identified headache and the alleged factors contributing to the development of headache.

Results: A total of 510 participants with a diagnosis of Covid-19 took part in the survey. Among the survey participants, 40.6% report headache as one of the main symptoms of Covid-19. 67.6% had a headache for the first time, 32.4% had it before. 33.8% – with a hypoxic state (a decrease in the level of saturation), 16.4% with taking medications, 5.4% believe that headaches occurred against the background of an asthenodepressive state in conditions of forced restrictions and self-isolation. The vast majority of patients with Covid-19- 72% reported that the headaches that occurred during the infection were different. The respondents rated the intensity of headache before COVID-19 on the VAS scale by 4.2±3.1 points, during the disease by 6.3±3.2. Among the survey participants, there were also those who had headaches during the exacerbation of Covid-19 that were identical to previously existing episodes.

Conclusions: During a new coronavirus infection, both the appearance of a newly identified headache and a change in the existing one are observed.
REAL LIFE EXPERIENCE OF ONE YEAR TREATMENT WITH GALCANEZUMAB IN CHRONIC MIGRAINE WITH AND WITHOUT MEDICATION OVERUSE HEADACHE

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Background and Aims: To present real-life data regarding Galcanezumab in patients with chronic migraine (CM) and medication overuse headache (MOH) and to assess its one-year effectiveness.

Methods: We analyzed 26 patients (F22, M4, mean age: 53, migraine history: 38yrs) who failed at least 3 preventive therapies. Galcanezumab was administered monthly for 12 treatments (T1 through T12) with a loading dose of 240 mg and maintenance dose of 120mg. Two patients interrupted treatment for inefficacy at T7 and T9. We collected clinical data on headache features (diary), disability and allodynia (standardized questionnaires) at baseline and quarterly.

Results: Patients with a pattern reversal from chronic to episodic migraine (i.e.>50% responders) were 42% at T1, rising to 62% at T12. Super-responders (i.e.>75% responders) were 8% at T1, 21% at T12. All clinical parameters showed a significant improvement already at T1 and persisted over one-year treatment (Fig.1). An improvement in MIDAS and HIT-6 scores was detected from T3 (p<0.001), while allodynia intensity decreased significantly from T12 (p=0.03) (Fig.2). Only mild side effects were reported by 33% of patients (constipation, cutaneous reactions and fatigue).

Fig1 – Panel A Percentage of patients who experienced a pattern reversal from chronic to episodic (p <0.01 for all time points). Panel B Reduction in monthly total headache days and monthly acute medication doses and days of intake. Monthly headache days: T1-T3-T6-T9-T12 vs baseline p<0.01; monthly acute medication doses: T1-T3-T6-T9-T12 vs baseline p<0.02; monthly days of drug intake T1-T3-T6-T9-T12 vs baseline p<0.001. ANOVA for repeated measures and post-hoc test
Conclusions:: Galcanezumab is related to a high percentage of pattern reversal in difficult-to-treat patients, showing a significant improvement in clinical features already during the 1st month of treatment and in headache-related disability after a few months. Moreover, efficacy is maintained over the long-term showing a positive tolerability profile.
THE RELATIONSHIP BETWEEN DEPRESSION AND MIGRAINE IN PATIENTS TREATED AT THE NPZR

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Background and Aims:: Data from a cross-sectional study revealed a higher prevalence of chronic headache as well as a very low utilization of adequate medical care in first-generation Turkish immigrants in Germany¹. Depending on the study the prevalence of migraine in Germany in women is reported between 15% and 23% and in men between 4% and 11%². Research shows a high correlation between migraine and psychiatric diseases. Especially the prevalence of depression (OR 2.2) is significantly higher³. A proper treatment of mental disorders is vital for a successful outcome of migraine therapies. The purpose of this research was to investigate the occurrence of depression among Turkish patients with migraine and to find a possible correlation between demographic characteristics.

Methods:: This study has determined the level of depression among Turkish patients with migraine (n=154, treated between 2015-2021).

Results:: The results show that severe depression was present in 75% of Turkish patients. Female patients showed higher rates of depression in comparison to male patients but there were no significant gender and severity of depression differences. Employment and income status were the significant factors in Turkish patients with migraine. Severe depression was more common among unemployed (p<.001) and low-income status (p<.001) migraine patients.

Conclusions:: The results of this ongoing research show no significant gender variation but differences in demographic characteristics such as income and employment status and disease severity, which could add more insight into the therapy of migraine. 1 (Kavuk, et al., 2006), 2 (RKI Headache Report 2020), 3 (Gaul & Hans, 2016).
PROGRESSIVE IMPROVEMENTS IN EFFICACY AND DISABILITY WITH FREMANEZUMAB IN PATIENTS WITH MEDICATION OVERUSE AND INADEQUATE RESPONSE TO MULTIPLE MIGRAINE PREVENTIVE MEDICATION CLASSES

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Background and Aims:: Fremanezumab, a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has demonstrated efficacy for migraine prevention in patients with episodic or chronic migraine (EM or CM) with documented inadequate response to 2–4 classes of prior preventive migraine medications in the phase 3b FOCUS study. This subgroup analysis evaluated the efficacy of fremanezumab in patients with baseline medication overuse (simple analgesics ≥15 days/month of triptans, ergots, barbiturate- or opioid-containing analgesics ≥10 days/month).

Methods:: In the double-blind (DB) period (DBP) of the FOCUS study, patients were randomized (1:1:1) to quarterly fremanezumab (675 mg subcutaneous [SC]), monthly fremanezumab (225 mg SC), or matched monthly placebo. For the open-label extension (OLE), all patients received monthly fremanezumab (225 mg SC). Results from the OLE were stratified by DB randomization group. Assessments included change from baseline in monthly average number of migraine days (MMDs), and disability scores (6-item Headache Impact Test [HIT-6] and Migraine Disability Assessment [MIDAS]).

Results:: During the DBP, for patients with medication overuse (427/838), fremanezumab treatment resulted in significant least-squares mean reductions in MMDs versus placebo (quarterly fremanezumab, −3.2; monthly fremanezumab, −4.4 vs placebo, −0.4; P≤0.0002), which increased during the OLE (mean: quarterly fremanezumab, −5.1; monthly fremanezumab, −6.0; placebo, −5.8). Significant improvements in HIT-6 and MIDAS scores versus placebo were also observed during the DBP (P≤0.0239); reductions increased through the OLE.

Conclusions:: Quarterly and monthly fremanezumab treatment demonstrated increasing efficacy and reductions in disability in patients with difficult-to-treat migraine and headache medication overuse.
REVERSION FROM MEDICATION OVERUSE WITH FREMANEZUMAB TREATMENT IN PATIENTS WITH INADEQUATE RESPONSE TO MULTIPLE MIGRAINE PREVENTIVE MEDICATION CLASSES

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Background and Aims:: Fremanezumab, a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has demonstrated efficacy for migraine prevention in patients with documented inadequate response to 2–4 prior preventive medication classes in the phase 3b FOCUS study. The aim of this subgroup analysis was to evaluate reductions in acute medication use in patients treated with fremanezumab with baseline medication overuse (MO; any acute medication ≥15 days/month or triptans, ergots, or combination medications ≥10 days/month).

Methods:: In the double-blind (DB) period (DBP) of FOCUS, patients were randomized (1:1:1) to quarterly fremanezumab, monthly fremanezumab, or placebo. All patients completing the DBP entered the open-label extension (OLE) and received monthly fremanezumab; results from OLE are stratified by DB randomization group. Changes from baseline in monthly average days of acute medication use and proportions of patients reverting to no MO were evaluated.

Results:: Among patients with MO (427/838), significant reductions in acute medication use were observed with quarterly (least squares mean change, −3.8) or monthly (−4.7) fremanezumab during the DBP, compared to placebo (−0.7; P<0.0001); reductions increased in the OLE (quarterly fremanezumab, −6.1; monthly fremanezumab, −6.9; placebo, −5.0). A greater proportion of patients reverted to no MO with quarterly and monthly fremanezumab, respectively, during the DBP versus placebo (39% and 42% vs 13%); an even greater proportion reverted during the OLE (quarterly fremanezumab, 48%; monthly fremanezumab, 46%; placebo, 41%).

Conclusions:: For patients with prior inadequate response to multiple preventive migraine medication classes and MO, fremanezumab reduced acute headache MO.
EFFICACY AND TOLERABILITY OF FREMANEZUMAB FOR MIGRAINE PREVENTIVE TREATMENT IN KOREAN PATIENTS WITH CHRONIC OR EPISODIC MIGRAINE

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Background and Aims:: Fremanezumab, a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has demonstrated efficacy in patients with chronic and episodic migraine (CM and EM). Efficacy and tolerability of fremanezumab for migraine preventive treatment in Korean patients with CM and EM have been evaluated in two randomized, double-blind, placebo-controlled phase 2b/3 clinical studies and compared with data from pivotal phase 3 HALO CM and HALO EM studies.

Methods:: The two phase 2b/3 studies had the same design as the pivotal HALO studies; patients were randomized (1:1:1) to quarterly or monthly fremanezumab or matched placebo for 12 weeks. For the CM and EM studies, respectively, primary efficacy endpoints were changes from baseline in monthly headache days of at least moderate severity (MHD) and monthly migraine days (MMD) during the 12-week treatment period.

Results:: For Korean CM (n=89) subgroup, least-squares mean reductions from baseline in MHD over 12 weeks with fremanezumab were comparable to those observed in the overall HALO CM study (Table). For Korean EM subgroup (n=54), least-squares mean reductions from baseline in MMD over 12 weeks with fremanezumab were also comparable to those observed in the overall HALO EM study (Table). Proportions of patients with ≥50% reduction in MHD or MMD was comparable in the Korean subgroups and pivotal studies (Table). No safety signals were identified in Korean subgroups.

Conclusions:: Although numbers of patients in Korean subgroups were small, there were trends in favor of fremanezumab for all endpoints analyzed, and fremanezumab was well tolerated.
ALTERED THALAMO CORTICAL CONNECTIVITY IN EPISODIC MIGRAINE: A RESTING STATE EXPLORATORY FMRI STUDY

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Background and Aims:: Migraine is a heterogeneous disorder characterized by an altered sensory processing where the thalamus is known to play a leading role. To further investigate the extent of the specific role of the thalamus in migraine, we used resting-state functional MRI (rs-fMRI) to evaluate the functional connectivity (FC) of the thalamic subnuclei within the pain matrix network during the migraine inter-ictal phase.

Methods:: In this exploratory study we enrolled 10 patients with episodic migraine (EM, 8 female, 44.3±10.6 yrs of age, 11.7±12.0 migraine days/month, MIDAS score 44.4±31.5) and 5 healthy subjects (3 female, 36.2 ±8.7 yrs of age). All subjects underwent a rs-fMRI scan in a pain free condition. Individual pre-processed rs-fMRI data were analysed with a seed-based correlation approach (SCA). All the thalamic subnuclei were chosen as regions of interest. Functional connectivity (FC) was calculated between each seed region and the rest of the pain matrix network, involving the salience network and the brainstem. Resulting maps were statistically compared between groups using a non-parametric permutation test. A statistical threshold of p<0.05 was considered significant.

Results:: Compared to healthy subjects, EM showed reduced FC between the ventral posterior nuclei (VPN) and insula, dorsal pons, prefrontal cortex and posterior cerebellum. Moreover, EM presented increased FC between bilateral pulvinar and the dorsal pons, the prefrontal and the posterior cingulate cortex.
Conclusions: These results suggest that the VPN and pulvinar, which are part of the cerebral functional circuitries implicated in pain processing, are differently orchestrating brain activity between healthy subjects and migraineurs also during the inter-critical phase.
RELATIONSHIP BETWEEN SLEEP DISORDERS AND LIFE-STYLE IN PATIENTS WITH CHRONIC TENSION-TYPE HEADACHE.

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Background and Aims:: Many epidemiological studies have evaluated on this association in relation to nonspecific headache, whereas relatively few epidemiological studies have focused on the specific diagnosis of tension-type headache (TTH) which is associated with sleep disorders and bad quality of life. This study is aimed to assess the prevalence and impact of sleep disturbances and its associations with life-style including work, social functioning and well-being in TTH patients.

Methods:: We examined 80 patients (men-36, 45%; women - 44, 55%) aged from 20 to 58 years in TTH patients at the Tashkent Medical Academy in neurology department. The Pittsburgh questionnaire was used for determining the quality of sleep index (PSQI). Headache-related life-style was measured using the following scales: Medical Outcomes Study Short Form, Disability Days/Impairment Ratings, The Hassles Scale Short Form.

Results:: On the Pittsburgh scale, various sleep disorders were observed in 65 patients (81%) of cases from 1 to 5 times a week in relation to the duration of sleep, daytime dysfunction, and subjective sleep quality (p<0.005). Poor sleep quality (higher PSQI components 22-29 points) were observed in patients with TTH. Significant impairments in functioning and well-being were evident in chronic tension-type headache and were captured by each of the assessment devices. Headache-related disability days were reported by 84% of patients (p<0.0001), work or social functioning was severely impaired in 58% of patients (p<0.005). Concerning sleep quality, the greater sleep scores were the worse life-style would be.

Conclusions:: The presence of association of headache and sleep disorders was found and it impacts negatively on patient's life-style. A close attention to sleep problems among patients with headache may have implication for the choice of treatment and the prognosis, possibly preventing chronicification of headache disorder and worse quality of life.
FREMANEZUMAB IMPROVES QUALITY OF LIFE IN PATIENTS WITH HIGHER- AND LOWER-FREQUENCY CHRONIC MIGRAINE

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Background and Aims:: Patients with migraine may experience increased disease burden as migraine frequency increases. Fremanezumab, a fully-humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has been shown to have significant effectiveness for migraine prevention. This pooled analysis assessed disability and quality-of-life (QoL) outcomes in patients with higher-frequency chronic migraine (HFCM; ≥19 monthly migraine days [MMDs]) or lower-frequency chronic migraine (LFCM; 15-18 MMDs) treated with fremanezumab from 2 double-blind phase 3 trials.

Methods:: In HALO CM and FOCUS, patients were randomized 1:1:1 to receive quarterly fremanezumab, monthly fremanezumab, or placebo. QoL and disability outcomes were assessed during the 4 weeks after the third dose of study drug by change from baseline in Migraine-Specific Quality of Life (MSQoL) domain scores and 6-Item Headache Impact Test (HIT-6) scores, respectively.

Results:: These analyses included 500 patients with HFCM and 511 with LFCM. Least-squares mean changes from baseline in MSQoL role-function restrictive scores were significantly greater with fremanezumab versus placebo in HFCM (quarterly, 16.2; monthly, 15.9; placebo, 8.1; $P\leq0.0006$) and LFCM (quarterly, 19.8; monthly, 20.6; placebo, 14.2; $P\leq0.0083$) subgroups, as were changes in role-function preventive (RFP) and emotional function scores for LFCM subgroup (both regimens; $P\leq0.0434$) and changes in RFP (both regimens; $P\leq0.0170$) for HFCM subgroup. Reductions from baseline in HIT-6 scores were significantly greater with fremanezumab (HFCM: quarterly, −4.5; monthly, −5.0; placebo, −3.3; monthly, $P=0.0169$; LFCM: quarterly, −5.6; monthly, −6.2; placebo, −3.8; both $P\leq0.0108$).

Conclusions:: QoL and disability were improved with fremanezumab versus placebo in patients with LFCM and HFCM.
Background and Aims:: White matter hyperintensity (WMH) in migraine could be related to inflammatory and antioxidant events. The aim is to verify whether migraine patients with WHM carry a genetic pro-inflammatory/pro-oxidative status.

Methods:: We compared lymphotoxin alpha (LTA) and superoxide dismutase1 (SOD1) and 2 (SOD2) gene polymorphisms (SNPs) in patients affected by episodic (EM) and chronic (CM) migraine and in unrelated healthy controls, and in migraine patients with (WMH+) and without WMH (WMH-) at brain magnetic resonance imaging (MRI).

Results:: We studied LTA, SOD1 and SOD2 polymorphisms in 370 consecutive patients (EM: 251; CM: 119) and in 100 controls. Brain MRIs were available in 183/370 patients (49.5%). Genotypes and allele frequencies did not differ between patients and controls. A strong linkage disequilibrium emerged between the two LTA (D'= 0.96, r= 0.29), but not among LTA and SOD1/SOD2 SNPs. The CAAC haplotype showed a significant trend toward a protective effect in migraine [OR= 0.49 (95% C.I.: 0.25–0.98), p=0.044]. No association was found between single SNPs or haplotypes and sex, migraine type, cardiovascular risk factors or disorders. The rs2071590T and the rs2234694C alleles were both associated with WMH (OR= 2.2; p=0.034; OR= 4.9; p=0.003). A four-loci haplotype (TGCT haplotype: rs2071590T/rs2844482G/rs2234694C/rs4880T) was significantly more frequent in WMH+ compared to WMH- (OR=8.7, p=0.009), being present in 7/38 (18.4%) WMH+ patients compared to 4/134 (3.0%) WMH- (p=0.003).

Conclusions:: A TGCT haplotype is independently associated with an increased WMH risk, suggesting that WMH could arise from an imbalance between migraine-related inflammatory/oxidative events and specific LTA and SOD1/SOD2 genotypes.
REAL-LIFE ASSESSMENT OF ERENUMAB DISCONTINUATION FOLLOWING ONE YEAR OF TREATMENT IN MIGRAINE PATIENTS

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Background and Aims: Monoclonal antibodies (mAbs) against CGRP are first-in-class drugs for migraine prevention, yet studies on treatment discontinuation are currently lacking. Real-life data are warranted to create up-to-date guidelines on migraine prevention with mAbs.

Methods: We prospectively recruited migraine patients who stopped erenumab after completion of one-year treatment. We aimed to assess changes in monthly headache days (MHD) and monthly pain medication intake (MPMI) at the last month of therapy (LMT), and, thereafter, at one (M1) and two (M2) months following treatment discontinuation.

Results: Eighty-eight patients were included. At LMT, MHD decreased from 21±6.9 to 10±7.6 (p<0.001), while MPMI decreased from 29±23.6 to 11±6 (p<0.001). MHD and MPMI following erenumab discontinuation were persistently lower compared to baseline, yet higher than LMT (M1: MHD=13±7.6, MPMI=18±15; M2: MHD=14±8; MPMI=19±15.6. p<0.0001). Additionally, compared to LMT, 34% (n=30) and 39% (n=34) of the patients showed a ≥50% worsening of MHD at M1 and at M2, respectively. However, only 10% (n=9) at M1, and 24% (n=21) at M2, of the population study showed a significant MHD worsening compared to baseline.

Conclusions: Erenumab discontinuation following successful one-year treatment tends to worsen migraine frequency, yet without reaching pre-treatment levels. Nonetheless, a subgroup of patients showed scarce persistent benefit after treatment discontinuation. Further studies are needed to assess risk factors for migraine worsening after discontinuation.
EFFICACY OF FREMANEZUMAB IN PATIENTS WITH CHRONIC AND EPISODIC MIGRAINE STRATIFIED BY MIGRAINE FREQUENCY

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Background and Aims:: Chronic and episodic migraine (CM/EM) can be characterized by frequency: low-frequency (LF), moderate-frequency (MF), or high-frequency (HF). This pooled analysis evaluated efficacy of fremanezumab, a fully humanized monoclonal antibody (IgG2Δα) that selectively targets the calcitonin gene-related peptide (CGRP) pathway, in patients with CM or EM by baseline migraine frequency.

Methods:: Patients from three phase 3 trials (HALO EM, HALO CM, and FOCUS) were randomized 1:1:1 to quarterly fremanezumab, monthly fremanezumab, or placebo for 12 weeks. Changes in monthly average migraine days (MMDs), headache days of at least moderate severity (MHDs), and percentage of patients with a shift down of ≥1 frequency category were evaluated by baseline frequency category.

Results:: At baseline, 659 patients had MFEM (4-9 MMDs); 515, HFEM (10-14 MMDs); 511, LFCM (15-18 MMDs); and 500, HFCM (≥19 MMDs). At 12 weeks, least-squares mean (SE) reductions from baseline in MMDs were significantly greater with fremanezumab versus placebo in patients with MFEM (quarterly, −3.5[0.22]; monthly, −3.4[0.22]; placebo, −1.5[0.21]; P<0.0001), HFEM (quarterly, −4.2[0.35]; monthly, −4.7[0.35]; placebo, −2.8[0.35]; P≤0.0009), LFCM (quarterly, −5.9[0.50]; monthly, −5.9[0.48]; placebo, −3.2[0.51]; P<0.0001), and HFCM (quarterly, −4.6[0.52]; monthly, −5.5[0.52]; placebo, −2.9[0.52]; P≤0.0078). Reductions in MHDs and proportions of patients with ≥50% reduction in MMDs were also significantly greater for fremanezumab versus placebo for all 4 subgroups (P≤0.0007 and P≤0.0464, respectively). Fremanezumab demonstrated increases in percentages of patients with ≥1-frequency category reduction versus placebo across all frequency category subgroups.

Conclusions:: Fremanezumab reduced MMDs, MHDs, and migraine attack frequency in patients with varied baseline migraine frequency.
IMPACT OF CALCITONIN GENE-RELATED PEPTIDE RECEPTOR ANTAGONIST ON QUALITY OF LIFE

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Background and Aims:: Migraine is a neurological condition that can interfere with every aspect of daily life. The calcitonin gene-related peptide receptor (CGRP) antagonists, such as Erenumab, bring a novel therapeutic approach to migraine management. This study aims to evaluate the Quality of Life (QoL) and mood in a sample of patients diagnosed with migraine and prophylactically treated with Erenumab.

Methods:: We offered Erenumab subcutaneously every 28 days to migraine patients, who referred unsatisfactory response to conventional prophylactic treatments. Patients were followed for nine months. Outcome measures, recorded at baseline (T0) and thereafter every 3 months (T1, T2, T3), included evaluation of the number of migraine episode/month, of disability through Migraine Disability Scale (MIDAS), of pain perception with the Visual Analogue Scale (VAS), of QoL with SF-36 questionnaire, and of mood with Back Inventory Depression (BDI) scale II.

Results:: We analyzed 27 patients (23 women), aged 45.33±9.72 years with a disease duration of 32.37±9.20 years. We observed a statistically significant difference from T0 to T3 regarding the number of migraine episodes (24.74±7.14 vs 8.52±8.03, p <0.01), the disability evaluated through MIDAS (32.78±17.32 vs 7.48±10.17, p <0.01), the QoL with SF-36 questionnaire (42.99±15.90 vs 63.11±20.26, p < 0.01) and the mood evaluated through BDI-II (16.04±10.09 vs 9.33±8.04, p <0.01). No significant differences occurred in the pain perception evaluation from T0 to T3 (8.61±0.78 vs 5.67±1.77, p >0.01).

Conclusions:: Erenumab is effective in patients with migraine refractory to conventional prophylactic treatments, as it reduces the frequency of migraine, and increase the QoL and the mood.
Quantitative EEG Recording of a Migraine Attack

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Background and Aims:: Records of EEG during the post ictal period of migraine attack usually show electrical abnormalities of cortical activity mostly related to unspecific symptoms as drowsiness or hyperventilation. However, patients have abnormal EEG rhythms also during the visual aura with an overall slow activity and variation in power spectral values due to a decreased alpha activity in the posterior leads with an increased theta and delta power in the frontocentral regions mimicking some features of true epileptic patients.

Methods:: We address this issue by showing a case of a 15 years old girl that during an EEG recording, started to complain a visual and sensory aura followed by a severe unilateral pulsating pain. EEG trace was acquired and record was cut it in time blocks of 20 seconds each one and analyzed, block by block, by employing quantitative EEG (qEEG) technique. In each block spectrum frequencies for all cortical area were isolated and compared with a basal recording obtained from the same patient.

Results:: EEG traces were analyzed considering spectrum frequencies and delta, theta and alpha activities were isolated. QEEG showed an increase of slow rhythms during the aura in the posterior leads and a subsequent immediate recovery of fast rhythms in the pain phase recorded in the same locations. Fast rhythms are equally represented in both phases.

Conclusions:: This kind of EEG pattern seems to suggest further possible physiological connections between mechanism of spreading depression and electrical brain activity and may shed new light on pathophysiology of migraine.
SECONDARY EFFICACY OUTCOMES OF TOP-PRO STUDY: A RANDOMIZED DOUBLE-BLIND CONTROLLED TRIAL OF TOPIRAMATE VERSUS PROPRANOLOL FOR PREVENTION OF CHRONIC MIGRAINE

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Background and Aims:: We conducted TOP-PRO-study, a double-blind RCT, to know whether propranolol is as efficacious as topiramate for the prevention of CM. In this paper, we report the secondary efficacy outcomes. Primary efficacy outcome showing the non-inferiority of propranolol have been described in another paper.

Methods:: CM patients aged above 18 years and less than 65 years of age, not on any preventive treatment were randomly allocated to receive topiramate (100 mg/day) or propranolol (160 mg/day). Secondary outcomes were mean change per 28 days at the end of 24 weeks compared to baseline in headache days, acute migraine treatment (AMT) days, visual analog scale (VAS) scores, headache impact-6 (HIT-6) scores, migraine specific quality of life (MSQOL) score and achievement of more than 50% reduction in headache days.

Results:: COVID-19 pandemic and lockdown halted the recruitment before the trial reached the planned sample size of 244. Of the 175 randomized patients, 95 (topiramate 46 and propranolol 49) completed the trial. The two groups were matched in terms of age, sex and baseline headache parameters. At the end of 24 weeks, both groups showed similar mean improvements in headache days per 28 days (-7.7 vs -7.8; p=0.928), >50% responder rate (32.6% vs 34.7%), AMT days (-6.7 vs -7.0; p=0.835), VAS score (-1.7 vs -2.2; p=0.355), HIT-6 score (-5.2 vs -7.3; p=0.153), MSQOL score (-5.8 vs -9.3; p=0.098).

Conclusions:: Propranolol was as efficacious as topiramate for the prevention of CM as assessed by multiple secondary outcome parameters. (Academic study: Clinical Trials Registry-India CTRI/2019/05/018997)
ANXIETY-DEPRESSIVE DISORDERS IN WOMEN WITH MIGRAINE.

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Background and Aims:: This research examines anxiety and depressive disorders in women with migraine.

Methods:: assessed the emotional sphere, the Spielberger test, the modification of Khanin, Beck Depression Scale Inventory.

Results:: 32 women with migraine were examined (2 groups: migraine without aura - 24 (75%) and migraine with aura - 8 (25%)). The control group consisted of 22 healthy women. Analysis of the emotional sphere showed that increased anxiety and decreased mood were found in 26 (81%) and 6 (19%) patients with migraine, respectively. The average score of reactive anxiety (RA) and personal anxiety (PA) in patients significantly exceeded the indicator of healthy subjects. Moderate or high anxiety was noted in 25 (82%) women, 7 (18%) had normal RA and PA. Depression was observed in 19 (59%) patients, of whom 8 (42%) were moderate and 11 (57%) were severe. It was investigated that in patients with wakefulness migraine at a relatively younger age, sleep disturbances and autonomic disturbances in the interictal period (IP) are less often observed. These patients have relatively low levels of anxiety (RA - 32, PA - 40), depression (14), and satisfactory health in the IP. Patients with sleep migraine are significantly older, characterized by a high frequency of autonomic disorders, the presence of persistent sleep disturbances in the IP, significantly higher (p = 0.02) levels of depression (24 points) and anxiety (RA - 36, PA - 50), which determines significant maladjustment of these patients in the IP.

Conclusions:: Women with migraine are characterized by a severe course of the attack, they are also characterized by a higher level of anxiety and depression.
INTERICTAL FRONTAL LOBE DYSFUNCTIONS IN EPISODIC MIGRAINE: A CLINIC BASED STUDY

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Background and Aims:: Episodic migraine (EM) patients often complain of interictal cognitive difficulties. We aimed to study interictal frontal lobe functions in EM patients and compare them with healthy controls without headaches.

Methods:: Consecutive EM patients diagnosed by ICHD-3 were studied. Demographic variables and various headache related parameters were noted. Minimental state examination (MMSE) was used for cognitive screening and frontal assessment battery (FAB) for assessing frontal lobe functions in cases and controls.

Results:: 122 EM patients (mean age: 29.1±8.5 years; 27M: 95F; mean illness duration 57.6±54.3 months) and 122 healthy controls (mean age: 29.1±4.7 years, 28M: 94F) were studied. Mean migraine days were 5.4±2.7 days/month. Mean headache duration was 14.3±14.2 hours. Mean headache severity, headache impact score and headache disability score were 7.0±1.4, 60.3±5.8, 13.1±8.6 respectively. Psychiatry co-morbidities were seen in 48/122 (39.3%) patients and in 25/122 (20.5%) controls (p=0.0021). Mean Epworth Sleepiness score in patients and controls were 3.9±2.1 and 2.9±1.8 respectively (p<0.0001). Mean MMSE score in patients and controls were 27.5 and 27.7 respectively (p=0.53). FAB score was significantly low in EM (14.4±2.0) as compared to healthy controls (16.1±1.3) [p<0.0001]. Components of FAB showed significant differences in lexical fluency (p<0.0001), motor series programming (p=0.0119), conflict (p<0.0001) and go-no-go (p<0.0001). Presence of psychiatric co-morbidities did not have significant impact on FAB.

Conclusions:: EM patients had significant interictal frontal lobe dysfunctions especially involving mental flexibility, motor planning and inhibition & interference control. These deficits may increase their disability and can have a bearing in their quality of life.
GREATER OCCIPITAL NERVE INJECTION IN CLUSTER HEADACHE: WHICH PROTOCOL TO CHOOSE? A COMPARISON STUDY

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Background and Aims:: Several Greater Occipital Nerve (GON) injections protocols are described for treatment of cluster headache (CH), and it is uncertain which leads to better results. Aim of this study is to compare two of most widely-accepted GON injections protocols: repeated suboccipital steroid injections and single GON anaesthetic blockade (GONB).

Methods:: We enrolled patients accessed for CH within 7 days from attacks-recrudescence. At first admission, patients received three repeated suboccipital injections (RSI) of slow-release methylprednisolone (srMP) 60mg on alternate-days. In the subsequent recrudescence-period and at least after 6 months, the same population received GONB with srMP 80 mg and lidocaine 40 mg. Primary outcome was the absence of CH-attacks at one-month. Secondary outcome was reduction of at least 50% of daily-attacks.

Results:: Fifteen patients were enrolled: 11 with episodic and 4 with chronic-CH. Nine patients (60%) were attacks free at one month after RSI, and 6 (40%) after GONB (p=0.27). Secondary outcome was reached in 12 patients (80%) after RSI and in 10 (67%) after GONB. Only mild adverse-events (AE) (stiffness/pain) were reported: more common with RSI (53%vs27%). Asked patient preference, 60% choose the RSI due to higher-rate and faster response.

Conclusions:: This is the first study comparing two GON injections protocols in the same CH population. RSI protocol showed a better response than GONB and was preferred by patients, even though the higher incidence of AE. However, no statistical superiority of one treatment was highlighted, and the choice must consider logistic, tolerability and patient preference. Further studies are needed to confirm these preliminary findings.
ASSESSMENT OF QUALITY OF SLEEP AND INSOMNIA IN MIGRAINE PATIENTS: A CLINIC BASED CASE CONTROL STUDY USING CLINICAL TOOLS

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Background and Aims: Migraine patients complain a wide spectrum of sleep disorders. We aimed to assess sleep quality and insomnia in migraine patients by using three clinical tools and compare the diagnostic yield of each.

Methods: Consecutive preventive drug-naive migraine patients diagnosed by ICHD-3 (aged >18 to <65 years) and age and sex-matched non-headache healthy controls were studied. We administered them a screening sleep questionnaire, a standardized 7-day sleep diary and Pittsburgh sleep quality index (PSQI) scale.

Results: Seventy migraine patients (mean age: 33.48 ±10.25 years; 9M: 61F; mean illness duration 64.18 ± 46.60 months) and 35 healthy controls (mean age: 34.14±9.41 years, 6M: 29F) were studied. Greater number of migraineurs demonstrated a poor quality of sleep as compared to healthy controls by the questionnaire method (82.9 % vs 25.7 %), by sleep dairy (62.8 % vs 14.2%) and by PSQI (abnormal global score >5 in 87.1 % vs 2.8 %). Insomnia was reported by 62.9% of migraineurs by the questionnaire method. Sleep dairy recorded 45.7% of migraineurs taking > 30 min of time to fall asleep & 57.4% having total sleep time <6 hours at night. The global PSQI score was significantly higher in migraineurs compared to controls [8.94± 4.00 vs 1.51 ±1.14 (p=<0.0001)]. The component scores of PSQI were also worse among the migraineurs.

Conclusions: Migraineurs had a greater magnitude of poor sleep quality and insomnia as compared to controls. For the detection of poor sleep quality and insomnia, all three instruments performed well; however, PSQI had the highest yield.
Background and Aims:: Estimations are that 60% of women who suffer from migraines experience attacks that are associated with menstruation. Menstrual migraines are typically more debilitating, more painful, and of longer duration. Menstrual migraines are mainly managed by the same pharmacological treatments as non-menstrual migraine, however these treatments are less effective for menstrual migraine attacks. Remote electrical neuromodulation (REN) is a non-pharmacological abortive treatment for migraine headache. The current analysis is the first to explore REN's effectiveness and tolerability in menstrual migraine. The current study evaluated the self-reported effectiveness and tolerability of REN for the acute treatment of menstrual migraine.

Methods:: This was a retrospective, observational survey study. Participants completed a short online survey assessing effectiveness, satisfaction, and tolerability outcomes.

Results:: Ninety-one participants qualified for the analysis, out of which 74.7% (68/91) reported that the treatment was at least moderately effective (moderately effective 37.4%, very effective 26.4%, extremely effective 11.0%). Additionally, 45.1% (41/91) reported satisfaction from remote electrical neuromodulation (slightly satisfied 33%, extremely satisfied 12.1%), while 34.1% were neutral and 20.9% (19/91) were not satisfied. Lastly, 100% of the participants reported that the treatment is at least moderately tolerable (moderately tolerable 8.8%, very tolerable 20.9%, extremely tolerable 70.3%), and 13.2% (12/91) reported mild short-term side effects.

Conclusions:: Remote electrical neuromodulation was reported as effective for menstrual migraine by most participants, and was very well tolerated. Remote electrical neuromodulation may thus provide a safe, non-pharmacological alternative for the acute treatment of menstrual migraine.
GENDER TYPES OF MIGRAINE

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Background and Aims:: Background: Migraine is considered mostly a woman’s complaint, even if it affects also men. The gender-related differences of migraine hold clinical relevance too. Differences between men and women in certain reactions, including responses to painful irritation, are largely due not only to the biological characteristics of men and women, but also to the varying degrees of their masculinity and femininity. Aim. The aim of this review was to study gender in patients with migraine and summarize recent findings on this matter.

Methods:: Materials and methods. The gender of 84 patients with migraine was determined using Sandra Bem survey; the clinical picture was assessed by headache diary

Results:: Results. The examined women were dominated by feminine types of gender: 34 people belonged to the androgynous type and 36 - to the feminine type. Among the masculine types of gender, the undifferentiated gender was found only in 10 patients, and masculine - only in 4. When assessing the percentage of gender types in patients with migraine men and women, the following gender characteristics were established: men were relatively more likely to belong to the gender of the undifferentiated type (21.9 %) and less often - androgynous (34.4%), in women the shares of these types were 5.8 and 44.2%, respectively.

Conclusions:: Conclusions. The most severe clinical course was typical for patients with undifferentiated gender characteristics. The most favorable clinical course was observed in the group of androgynous patients with migraine
THE ASSESSMENT OF THE SEVERITY OF HEADACHES CAUSED BY TEMPOROMANDIBULAR DISORDER. A DESCRIPTIVE ANALYSIS FROM THE MON-TIMELINE STUDY

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Background and Aims:: Temporomandibular disorders (TMD) are associated with various types of headaches; not only contributing to their development, also affecting their frequency and intensity. Headaches are one of the most common conditions affecting the general population. We studied the association between temporomandibular joint (TMJ) symptoms as the indication of TMD and headaches, in order to determine whether TMD are associated with headaches.

Methods:: This study is based on sub-samples of individuals residing in Ulaanbaatar from the Mon-TimeLine nationwide survey data. A total of 1087 participants, aged 13-65, were randomly selected. The temporomandibular characteristics were evaluated by professional orthodontists via a medical examination and a questionnaire. The headache assessment was undertaken by a neurologist via face-to-face interviews with the participants.

Results:: TMJ pain, TMJ sound, masticatory muscle pain (MMP), and difficulty during mouth opening (DDMO) were 13.7%, 28.4%, 11.8%, and 3.5%, respectively. In the sample population, the prevalence of headaches was 61.8% (n=672). Headache, whether defined as once a week or more or as moderate, severe, was significantly related to TMD pain. Severe headache showed stronger associations with TMD than between moderate and mild headache.

Conclusions:: In terms of headache characteristics, people with TMJ pain and MMP, the headaches were localized to the temporal region, and the pain level was stronger when compared to people without TMJ symptoms. In conclusion, headache appears to independently and highly associated with TMD pain in adults. Therefore, our study reveals the needs for further investigations, especially in people with TMD, to fully elucidate the problem of TMD management in Mongolia.
NEW DAILY PERSISTENT HEADACHE AFTER SARS-COV-2 INFECTION: A CASE SERIES

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Background and Aims:: The 2019 Coronavirus (SARS-CoV-2) is a novel respiratory virus which causes Coronavirus Disease 19 (COVID-19). Although the predominant clinical picture of COVID-19 is represented by respiratory symptoms, neurological manifestations are being increasingly recognized. Headache, in particular migraine-like and tension types, has been largely reported in patients suffering from COVID-19 both in the acute and the healing phase of the infection. New Daily Persistent Headache (NDPH) is a primary headache characterized by persistent and daily painful symptoms, with pain becoming continuous and non-remitting within 24 hours, and lasting more than 3 months. Even though an increasing number of reports describes patients who develop a persistent headache, diagnosis of NDPH has been rarely explored in the context of COVID-19.

Methods:: Two patients with persistent headache and Sars-CoV-2 infection were identified. Both underwent a full clinical and neuroradiological evaluation consisted on Computerized Tomography with angiography sequences and Magnetic Resonance of the brain. Blood sample with inflammatory biomarkers search was also performed.

Results:: According to International Classifications of Headache Disorders diagnosis of Probable New Daily Persistent Headache was made. The treatment with high doses of steroids was associated with relief of symptoms.

Conclusions:: Our report described two cases of probable NDPH due to SARS-CoV-2 infection. Clinical evaluation of COVID-19 patients presenting with persistent headache should take into consideration NDPH. Given the supposed major role for neuroinflammation in the genesis of Sars-CoV-2-driven NDPH, immunomodulatory therapy should be promptly started. In line with this hypothesis, we obtained a good therapeutic response to short-term high dose of corticosteroids.
PERIAQUEDUCTAL GRAY MATTER (PAG) IN MIGRAINE: TRANSCRANIAL SONOGRAPHY STUDY

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Background and Aims:: Periaqueductal gray (PAG) plays an important role in the modulation of descending pain control. Previous MRI studies showed that increased PAG iron levels in both episodic and chronic migraine patients correlated with disease duration. Transcranial sonography (TCS) is an imaging technique that allows visualization of heavy metals in the brain parenchyma as an area of hyperecogenicity. The PAG is the gray matter located around the cerebral aqueduct and usually ecographic signal of this region is indistinguishable from the adjacent parenchyma. Our aim was to investigate hyperechogenicity of PAG in migraine patients.

Methods:: TCS was performed with Esaote MyLab Twice ultrasound machine, applying the sonographic parameters according to international consensus guidelines used for Movement Disorders We investigated 13 patients with episodic migraine (EM), 15 with chronic migraine and medication overuse headache (CM+MOH) and 10 Healthy Controls (HCs). The area of PAG hyperechogenicity visualized through the transtemporal window was measured semiautomatically on each side and then calculated as a mean value.

Results:: PAG hyperechogenicity was visualized in 100% of the CM+MOH patients, 69% of EM patients and 44% of HCs (p <0.001). No significant difference was found in the hyperechogenic PAG area among the three groups (p=0.295). However PAG hyperechogenicity area correlated with disease duration (p<0.023), pain intensity (p<0.031) and scores of the HIT-6 scale (p<0.043).

Conclusions:: These preliminary data suggest that repeated migraine attacks may lead over time to increased oxidative stress and free radicals release, contributing to secondary damage, contextual hyperaemia, and iron deposit in the PAG.
Background and Aims:: Osmophobia, defined in medical dictionaries as a morbid fear of smells. Incidence based on the different diagnosis of headaches. Olfactory hypersensitivity, anxiety and pain share common neural pathways and area activation, a possible functional association and an interaction of one with the other might be argued, basing both on imaging data and on the clinical experience. The aim of this study was to investigate the relationship between osmophobia and clinical features in headache patients. It has been supposed that osmophobia play a role in the process of a central sensitization.

Methods:: This was an observational retrospective cohort study based on data collected in a headache center. We selected 1170 patients aged 18–65 years. Different clinical features were evaluated during the examination including: The migraine disability assessment (MIDAS), Allodynia Symptom Checklist, Self-rating Depression scale, Self-rating Anxiety scale, VAS, Fibromyalgia.

Results:: Osmophobia have a prognostic role during migraine chronicization. Significantly high is the correlation between osmophobia, pain intensity, allodynic migraineurs, length of headache history, anxiety and depression.

Conclusions:: The co-presence in patients of osmophobia and alldynia is one of the predictive indices to consider osmophobia as a central sensitization symptom. Osmophobic patients seems to have also more affective symptoms and that demonstrates that Osmophobia associated with sensory hyperactivity. All these aspects are linked to the migraine, seen as a process of cortical hyperactivity.
UNUSUAL ETIOLOGY OF CHRONIC HEADACHE

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Background and Aims:: Introduction: Chronic headaches are one of the main causes of our patients’ consultation in neurology. This variety of headaches remains largely poorly recognized. However, it is a major problem of public health by its frequency and its socio-economic impact. Through this work, the authors report a case of pachymeningitis revealing a Sjogren’s syndrome whose clinical manifestation was a change in the character of a chronic headache.

Methods:: Clinical case: A 69-year-old woman, without past history, hospitalized at the Department of Neurology for etiological assessment of aggravation of chronic headaches, they became more intense and resistant to analgesic treatment. Clinical examination was without characteristics. Brain MRI objectified pachymeningitis of the cerebral falx, the cerebellar tentorium, and the clivus, with extension to the cervical spinal canal, associated with an enlargement of cerebral ventricles. History taking revealed the existence of xerostomia and xerophthalmia. The accessory salivary gland biopsy objectified Chisholm stage IV sialadenitis, the search for anti-SSA antibodies and anti-SSB antibodies was positive. The diagnosis of primary Sjogren’s syndrome was retained.

Results:: The patient improved with corticosteroid therapy.

Conclusions:: Through In this observation, we highlight the importance to look behind chronic headaches resisted to symptomatic treatment, or in front of an unexplained change in its characteristics. Even if the association of pachymeningitis and Sjögren’s syndrome is rare, it seems logical to rule it out.
MIGRAINE IN MENOPAUSE - A CROSS-SECTIONAL STUDY IN A HEADACHE CENTER IN RIO DE JANEIRO, BRAZIL.

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Background and Aims:: Migraine mainly affects women in the reproductive years and the association between migraine and sex hormones, specifically estrogens, has induced the assumption that migraine would improve in menopause. However, while some studies found that migraine without aura would remit in menopause, others observed no changes in migraine activity after menopause. Here we aim to describe the characteristics of migraine in postmenopausal women.

Methods:: In August 2019, a headache center was inaugurated at our university hospital – Hospital Universitário Gaffrée e Guinle. All patients who subsequently attended this clinic were evaluated according to the diagnostic criteria from the International Classification of Headache Disorders, 3rd ed. Among the patients diagnosed with migraine, we have selected the women in perimenopause or menopause. Data were collected from medical records and further complimented with phone interviews. The cases were analyzed as to demographic and clinical variables, and as to putative risk factors.

Results:: Of 52 migraine patients, 12 (23.1%) were postmenopausal women. The mean age was 56.3 yrs (SD ± 4.0 yrs). Most of them (83.3%) had migraine without aura only. Ten patients (83.3%) had chronic headache. Medication overuse was observed in 50.0% of the cases. Half of them reported any mental disorder (predominantly mood disorders). Four patients (33.3%) had a past of smoking.

Conclusions:: Even migraine without aura might not subside in postmenopausal women. A tendency for chronic headache was also noted for this group, which could not be explained in half of the cases for medication overuse.
PATIENTS PRESENTED IN EMERGENCY DEPARTMENT OF SRD WITH HEADACHE AS SYMPTOM OF COVID-19

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Background and Aims:: To see the patients presented in the Emergency Department of SRD with headache as a symptom of COVID-19.

Methods:: We have seen frequency and characteristic of headache in 180 patients in an emergency with a test of polymerase chain reaction positive.

Results:: These patients are presented in period 1 August 2020 until 31 December 2020 with the headache as the first symptom of COVID – 19. The most of cases was reported in man 56% (101 patients) and mid-age of cases were 52.5 years. The most of patients 62% (112 patients) had a very severe intensity of headache and it was diffuse or more in the frontal area (in 90% of these groups). 38 % of patients had moderate headache, and a part of all patients 22% (40 patients) had characteristics of migraine with hemicrania and nausea and vomitus and photophobia (this was seen more in patients that had experience migraine before, p < 0.05). In 25% of all patients (45) had continuous headaches without a period of free pain even after administration of analgesic therapy. A part of patients 34 % (61 patients) had anosmia as accompanied symptom. All cases had seen by a neurologist that did suggestions for all examinations that were necessary.

Conclusions:: In our Department of Emergency, we have seen a closed correlation of headaches with COVID-19. The most of patients had headache the only symptom in the first days of covid-19 and it was in general severe, diffuse, and in some patients as a migraine phenotype.
CT PERFUSION IN ACUTE CONFUSIONAL MIGRAINE

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Background and Aims:: Acute confusional migraine (ACM) is a rare migraine variant characterized by headache associated with altered mental status and speech difficulties. A 50-year-old headache-suffer male was admitted to our Hospital due to severe headache, vomiting, confusion, agitation, disinhibition and dysphasia. He performed brain CT, CTA and CTP which showed hypoperfusion in the left temporal lobe without an ischemic core. All these symptoms completely resolved the following day, with residual amnesia for the episode. Laboratory blood test and cerebrospinal fluid analysis were normal. Brain MRI showed a puntiform hyperintensity on DWI in left parietal lobe, not confirmed on follow-up MRI. Baseline EEG showed diffuse left-side dominant slow waves, with subsequent improvement. ACM is a rare migraine variant and often a challenge for clinicians to diagnose appropriately, also because there are no classification criteria. It is an exclusion diagnosis and some dangerous causes of confusion (e.g., epilepsy, ischemia, hemorrhage, neoplasm and encephalitis) should be ruled out. Data from previous published reports showed that ACM is characterized by decreased cerebral blood flow in the left splenium region and medial temporal lobe on SPECT scans. In our patient we found hypoperfusion on the left temporal lobe without an ischemic core on brain CTP. The more widespread use of brain CTP in an acute setting together with clinical course and blood and CSF results could help physicians to raise the doubt of this rare clinical entity avoiding misdiagnosis or excessive diagnostic testing.

Methods:: see B and A
Results:: see B and A
Conclusions:: see B and A
CT BRAIN IMAGING FINDINGS AMONG THE HEADACHE PATIENTS - A RETROSPECTIVE STUDY OF 220 CASES.

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Background and Aims:: Headache is the most common complain of the patients presenting to Radiology department for the purpose of doing a CT scan of Brain.

Methods:: This retrospective study included all patients with the complaints of headache with or without other neurological symptoms and referred to Department of Radiology for CT scan of Brain from January to October 2018. Patients were divided into three groups based on CT scan findings: 1. Those with normal CT scan, 2. those with minor abnormality (not altering the patient management), 3. Those with clinically significant abnormality (altering the management protocol). Results were tabulated and analyzed from CT Brain imaging of patients with history of headache.

Results:: A total no of 220 patients were included from 668 patients in January to October 2018. Among them 128 had normal CT (58.18%) and 92 (41.82%) had abnormal CT findings of which major and minor abnormalities constitute 17.27% (eg. Acute cerebral infarction 14.08%) and 24.55% (eg. DCA 19.09%) respectively. Headache is common in both male (52.73%) and female (47.27%); most common age group affected is 41-60 years (35%).

Conclusions:: Abnormal CT in Headache patients is 41.82% at a district level hospital of Bangladesh indicates CT scan may play a vital role to rule out secondary cause of headache and help in further management.
THYROID STIMULATING HORMONE LEVEL IN MIGRAINE HEADACHE

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Background and Aims::

Migraine is a primary headache disorder, the second commonest cause after Tension headache with a female preponderance. There is complex pathophysiology of migraine and migraine related disorders. Research is going on regarding potential association between migraine and thyroid function. The aim of this study was to investigate the association between Thyroid stimulating hormone level and migraine in adults and also to evaluate association of demographic and headache characteristics of migraine with thyroid function.

Methods:: This cross sectional comparative study was done to investigate the association between thyroid stimulating hormone level and thyroid abnormalities in adults migraine patients. The study was conducted in Mymensingh Medical College Hospital, a tertiary level hospital of Bangladesh. Study period was from November 2017 to April 2018. The study subjects consisted of 50 patients with migraine headache as case, compared with 50 patients of headache other than migraine as control, seen in Neurology out patient department (OPD). Thyroid function test was performed in both groups.

Results:: Mean age was 29.80±9.87 years in migraine group and 34.18±11.82 years in non migraine group. Male female ratio was 1:2.3 and 1:1.7 in two groups. Level of TSH was significantly higher in migraine patients (3.52±2.53 vs. 2.25±2.13) than other headache patients (p=0.008). Thyroid disorder especially subclinical hypothyroidism was significantly higher (28% vs. 08%) in migraineurs than non migraineurs (p=0.032). No significant relationship was found between thyroid hormone level and headache characteristics of migraine patients (p>0.05).

Conclusions:: Migraine headache is associated with low thyroid stimulating hormone and thyroid disorder can be considered as comorbidity of migraine headache.
TREATMENT OF PERSISTENT POST-TRAUMATIC HEADACHE WITH ONABOTULINUMTOXINA: RESPONSE RATES ACCORDING TO CLINICAL PHENOTYPE

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Background and Aims:: Traumatic brain injury frequently is complicated by chronic headache which may have features of either chronic migraine (CM) or chronic tension-type headache (CTTH). We currently lack any evidence-based prophylactic therapy for persistent post-traumatic headache. In this study we assessed the efficacy, safety and tolerability of onabotulinumtoxinA in treating patients with persistent post-traumatic headache and stratified patients according to the clinical phenotype of their headache disorder (ie, CM vs CTTH)

Methods:: We randomized patients with persistent posttraumatic headache of at least 3 months duration to treatment with open-label onabotulinumtoxinA administered according to the PREEMPT dosing/injection paradigm. On the basis of the patient's history and using current ICHD-3 criteria, at baseline we assigned each patient a clinical phenotype for his/her headache disorder: CM or CTTH. We defined a positive treatment response as a 50% or greater decline in monthly headache frequency at month 8 of treatment relative to the pre-treatment baseline month.

Results:: Of 181 patients evaluated, 174 patients (96%) completed all 3 treatments. Clinical phenotype was CM in 116 (64%) and CTTH in 65 (36%). In the CM subgroup, significantly more patients (66/116: 57%) achieved the primary treatment endpoint than in the CTTH subgroup (14/65: 22%; p<.05).

Conclusions:: For patients with persistent post-traumatic headache, onabotulinumtoxinA appears to be more efficacious in those with a clinical phenotype of CM than in those with a phenotype of CTTH.
EVALUATION OF THE EFFECTS OF NON-PHARMACOLOGICAL INTERVENTIONS ON THE PSYCHOLOGICAL PROFILE IN ADOLESCENTS WITH TENSION-TYPE HEADACHE

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Background and Aims:: Some evidence suggests that heart rate variability biofeedback-based training (HRV-BBT) might be an effective way to treat headaches and psychological symptoms. The aim to examine the effect of non-pharmacological therapy (HRV-BBT and complex isometric exercises (IE)) on anxiety and depression in adolescents with tension-type headache (TTH).

Methods:: 118 adolescents (ages 13-18) were examined. We formed four groups of adolescents with episodic (ETTH) and chronic TTH (CTTH) who received only drug therapy and only non-drug therapy and 5th group – adolescents with CTTH who received a combination of drug and non-drug therapy. The intensity of the pain (VAS); the level of reactive and personal anxiety (self-esteem scale Spielberger-Hanin); the level of depression (scale of V.A. Zhmurova) were performed. Adolescents received conventional pharmacotherapy for 1 month. Non-drug therapy was in the form of HRV-BBT (10-12 sessions) and a complex of isometric exercises (IE).

Results:: We observed a decrease in the level of anxiety in adolescents with TTH after HRV-BBT. However, only the reduction in reactive anxiety was significant (ETTH: before/after treatment – 42,6±7,5/33,5±5,4, p<0,05; CTTH: 37,7±6,8/29,2±6,8, p<0,05). The level of depression was significantly reduced after HRV-BBT in adolescents of all groups (ETTH: before/after treatment – 20,2±4,7/14,4±3,9, p<0,05; CTTH: 24,9±5,3/9,4±3,8, p<0,05), and the use of pharmacotherapy had a positive effect (before/after treatment – 25,1±5,2/11,7±4,8, p<0,05) only in the group with CTTH (who more often received amitriptyline).

Conclusions:: Our findings support the beneficial impact of non-drug therapy (HRV-BBT and IE) on anxiety and depression for adolescents with TTH (with higher effectiveness in adolescents with episodic forms).
IMPACT OF RAMADAN FASTING ON MIGRAINE HEADACHE

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Background and Aims:: Fasting is known as a migraine trigger for migraine. We aimed to study the impact of fasting of The Holy month of Ramadan on episodic migraine.

Methods:: This retrospective study included patients diagnosed as migraine according to The International Classification of Headache Disorders, 3rd edition (ICDH-3). Both genders, aged between 18 and 65 years were included. Frequency, severity of migraine attacks and number of analgesic days during Ramadan were compared to those during Shaban, the Immediate previous month to Ramadan. Number of breaking fasting due to migraine was reported.

Results:: This study identified 293 with migraine with mean age and mean disease duration 37.09 ±9.36, 12.34±9.27 years respectively. Most of them were females(89.1%). During Ramadan, the patient had significant increase in migraine days 10.42±7.98 compared with 6.90±6.55 migraine days during the previous month (p < 0.001). Days of analgesic use (11.32±10.46 versus 6.11±6.69;P<0,001) and migraine severity (7.46±2.39 versus 6.84±2.25; P<0,001) were significantly increased during Ramadan compared to Shaban. A minority (1.7) of the patients could not tolerate fasting whole Ramadan and 36.5% broke their fasting for some days during Ramadan. Some patients changed previous prophylactic therapy before fasting to reduce the impact of fasting on migraine headache. Most of cohort (82.3%) continue on the same management plan for migraine during Ramadan. Majority of cohort (75.4%) reported that migraine interfered with their daily activities due to fasting during Ramadan.

Conclusions:: Ramadan fasting has negative impact on migraine patients. Physicians should educate migraine patients how to manage their headache and habits before starting fasting.
TRIGGERS OF MIGRAINE DURING COVID-19 PANDEMIC LOCKDOWN

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Background and Aims:: Lock down caused lifestyle changes and represented an impact on human health. Environmental factors can trigger migraine headache. We aimed to report the triggers of migraine attacks due to lifestyle changes during coronavirus disease 2019 (COVID-19) pandemic lockdown.

Methods:: This cross-sectional survey included patients diagnosed as migraine according to The International Classification of Headache Disorders, 3rd edition (ICDH-3). During the lockdown, we submitted an online self-reported web-based questionnaire to patients already diagnosed with migraine and attends headache clinic at Ibn Sina Hospital in Kuwait. Questions explored triggers of migraine headache attacks during COVID-19 Pandemic lockdown. Answers were transformed into data for statistical analysis.

Results:: A total of 340 migraine patients responded to questionnaire. The mean age of them is 34.65 years. Females were predominant 79.1%. Majority of the cohort 85 % has more than one trigger of migraine attack. The commonest triggers were smell of strong odors in 214 (62.9%), followed by certain food in 175 (51.8%), sleep disturbance in 120 (35.3%), Emotional or mental stress in 80 (23.6%), caffeine in 80 (23.6%), flickers of Light in 78 (22.9), weather changes in 68(20%), smoking in 65 (19.12), noise in 56 (16.5), sun light exposure in 41 (12.1), Fasting/ Hypoglycemia in 40 (11.7), hormonal changes in 37 (10.6%), physical excretion/fatigue in 24 (7.1), screen exposure in 20 (5.9%), and dehydration in 14 (4.1%).

Conclusions:: Lifestyle changes during lock down may negatively impact migraine through patients exposure to many triggers. Strong odors, food, sleep disturbance and stress were the most migraine triggers during COVID-19 lockdown.
OXYGEN THERAPY IN HEADACHE DISORDERS: WHAT IS KNOWN?

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Background and Aims:: The global active prevalence of migraines is approximately 14.7%. Oxygen therapy may reduce the use of Nonsteroidal anti-inflammatory drugs (NSAIDs) which often have various negative side effects. The purpose of this systematic review is to analyze the literature on the efficacy of high flow oxygen for the management of headache disorders, compared to placebo treatment.

Methods:: Studies were identified by PubMed, Web of Science and Scopus database from 1980 to the 30th of October 2020. The search included the following terms: “oxygen therapy” and “headache” and “migraine.” Studies were included if high flow oxygen was used in the treatment of headache disorders All selected studies were qualitatively analyzed.

Results:: Our literature search identified 71 studies, of which 65 were discarded and 6 were included in the meta-analysis. The random effect model did not show a pooled significant resolution of headache disorders (OR 2.08 (95% CI 0.92–4.70), p < 0.0001) in the oxygen therapy group compared to the placebo group.

Conclusions:: In our systematic review of six studies, there were no significant differences between high flow oxygen and placebo treatment groups.
CEREBRAL FAT EMBOLISM SYNDROME PRESENTING WITH A MIGRAINE ATTACK

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Background and Aims:: Fat embolism syndrome (FES) is characterized by cerebral, respiratory, and cutaneous manifestations following orthopedic trauma. Cerebral fat embolism (CFE) is a subtype of FES. We report a case of subarachnoidal fat embolism due to a sacral trauma presenting with a migraine attack.

Methods:: A 39-year-old Caucasian man (BMI 22) fell down accidentally with acute low back pain and progressive severe pulsatile headache. Admitted to the hospital, a brain CT showed multiple hypodense areas into the subarachnoid space. Hounsfield unit analysis demonstrated numbers compatible with fat. A brain MRI confirmed the presence of subarachnoid fat droplets. The sacral-coccygeal MRI showed a displaced fracture of the 5th sacral vertebra and inflammation of epidural fat. After three days he went home with symptomatic therapy.

Results:: To our knowledge it is the first case of subarachnoidal fat embolism presenting with a migraine attack.

Conclusions:: Migraine is a multifactorial disorder, which could be triggered by a specific injury. Typically CFE imaging is a “starfield” pattern on diffusion-weighted MRI due to the involvement of multiple small arteries. Fat present in the subarachnoid space is less common. Patient’s trauma caused the vertebral fracture, and probably allowed the epidural fat to enter into the subarachnoid space giving evidence of multiple subarachnoid fat droplets in the brain.
FAMILIAR HEMIPLEGIC MIGRAINE: A PRELIMINARY CLINICAL AND FOLLOW-UP STUDY IN A PEDIATRIC SAMPLE.

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Background and Aims:: Familial Hemiplegic Migraine (FHM) is a rare clinical condition characterised by headache and motor weakness often unilateral. Follow-up studies are even rarer and there is the need to increase the observations of pediatric population affected by FHM to better clarify the prognosis and possible treatment. Aim of our study was to carry out a follow-up activity in a group of 7 children affected by FHM.

Methods:: A multi-center study was conducted retrospectively to select all genetically proven cases of FHM, collecting data based on clinical and genetic documentation. The selected subjects were interviewed on clinical course of hemiplegic migraine, possible other types of headache and clinical disorders.

Results:: Our children were 5 males and 2 females (age media onset: 7ys 8m, range age 3,3-15,2; age media follow-up 13 ys 6 m; follow-up duration 5 ys 9 m., range 3ys4m -9ys). We found a CACNA1A mutation in 3 children and a ATP1A2 in 4. At the follow-up time they had complained 1.86 attacks for year. Moreover clinically 57% presented speech disorders, 28,57% sensory disorders, 14,28% visual disorders and 57,14% an impairment of consciousness. Otherwise only 1 child presented a diagnosis of epilepsy and intellectual disability. 3 children showed recurrent attacks of migraine with and without aura.

Conclusions:: Our data supports the recent data of other Italian multicentric studies on 14 subjects showing a low frequency of hemiplegic attacks. Further our cases were rarely associated to other disorders and had a good prognosis to short-term follow-up.
SEROTONERGIC DYSREGULATION: NEW INSIGHTS OF REVERSIBLE CEREBRAL VASOCONESTRICTION SYNDROME PATHOPHYSIOLOGY.

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Background and Aims:: The pathophysiology of RCVS is not yet fully understood. Several precipitating factors, such as serotonergic hyperactivity, have been associated to this transient disturbance in cerebrovascular tone control. We present two atypical cases that offer new insights on the etiological role of serotonergic regulation in RCVS.

Methods:: In the first case, a 38-year-old woman presented a postpartum, new onset, severe and excruciating headache followed by a mild and continuous daily headache. Transcranial Doppler showed mean increased velocities in left middle (Vmean 140 cm/s) and anterior (Vmean 120 cm/s) cerebral arteries that normalized after nimodipine treatment. Headache improved with amitriptyline preventive treatment. In the second case, a 52-year-old migraineur woman presented an unusual thunderclap headache, followed by sudden onset of aphasia and clumsiness of the right hand. Colour cervical Doppler showed an increased peak systolic velocity in the left distal internal carotid artery (VPS 140 cm/s) and carotid syphon (VPS 110 cm/s), which normalized after nimodipine. She suffered from tryptophan deficiency, the amino acid precursor of serotonin.
**Results:** Although amitriptyline primarily inhibits serotonin and norepinephrine reuptake, it allows in the first patient a progressive pain relief without worsening vasospasm, possibly due to its complex pharmacodynamic profile. Secondly, no other cases of RCVS associated with tryptophan deficiency are currently reported: its low levels, unlike an excess of serotonin, could promote endothelial dysfunction. 

**Conclusions:** RCVS may not be due to a merely increase in serotonergic tone, but more likely, to a dysregulation of serotonergic neurotransmission, leading to an abnormal brain vasoreactivity.
TREATMENT RESPONSES TO ERENUMAB IN ONABOTULINUMTOXINA-REFRACTORY CHRONIC MIGRAINE: LONG-TERM REAL-WORLD EXPERIENCE FROM A SPECIALIST HEADACHE CENTRE

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Background and Aims:: Erenumab is a novel humanised anti-calcitonin gene-related peptide (CGRP) receptor monoclonal antibody efficacious in chronic migraine (CM) prophylaxis. We investigate long-term real-world erenumab efficacy in converting OnabotulinumtoxinA-refractory CM to episodic migraine (EM).

Methods:: We measured monthly headache-days (MHD) and monthly migraine-days (MMD) in a real-world prospective study of 186 OnabotulinumtoxinA-refractory CM patients treated with erenumab for 23 months in a Chinese specialist headache centre. Mean MHD<15 and mean MMD<8 days/month responses assessed conversion to EM.

Results:: Mean baseline MHD and MMD were 26.2 and 18.6 days. 115 (61.8%) patients experienced no baseline headache-freedom. At Month 23, mean MHD and MMD reductions were 12.8 and 13.4 days (p<0.001). At Month 23, 79 (42.6%), 111 (59.7%) and 89 (47.8%) patients achieved mean MHD<15, mean MMD<8, and both outcomes; 50 (26.9%) and 41 (22.0%) patients achieved mean MHD<15 and MMD<8 between 6–19 months; whilst 152 (81.7%), 124 (66.7%) and 42 (22.6%) patients achieved >30%, >50% and >75% baseline MMD reduction. 45 (24.2%) achieved >30% response after >3 months. More patients with baseline headache-freedom achieved mean MHD<15 responses at Months 12 and 23 (Month 12: 76.1% vs 7.8%, 68.3% difference, p<0.0001; Month 23: 77.5% vs 20.9%, 56.6% difference, p<0.0001), and >50% baseline MMD reduction responses at Months 12 and 23 (Month 12: 95.8% vs 53.0%, 42.8% difference, p<0.0001; Month 23: 93.0% vs 50.4%, 42.6% difference, p<0.0001), than those without.

Conclusions:: Erenumab converts onabotulinumtoxinA-refractory CM to EM in the real-world over 23 months, with some delayed responders. Baseline headache-freedom heralded superior treatment responses.
ASSOCIATION STUDY BETWEEN HEADACHE AND DIZZINESS ACCORDING TO AGE SPECTRUM FOR PATIENTS

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**Background and Aims:** Patients with headache often experience various types of vertigo. And several studies have suggested an epidemiologic and physiologic association of headache and vertigo. Researchers have investigated the association between headache and vertigo. We investigate whether vertigo (peripheral vertigo or central vertigo) is correlated with clinical relevance in headache patients according to age spectrum.

**Methods:** From May 2020 to February 2021, 925 patients, aged ≥7 years and participants who met the inclusion criteria were enrolled from the neurology clinics. We re-analyzed patients who experience headache with/without vertigo symptoms and two groups were studied according to the patient’s age. Logistic regression analysis was used to evaluate the association between headache and vertigo. First, we reviewed vertigo with diagnosed 281 and 570 headache patients, and 31 vertiginous headache. Second, common types of primary headache patients were included. Third, the vertigo was classified into 2 groups: peripheral or central types.

**Results:** Of the 925 outpatient, headache of 570 (61.6%) and vertigo of 281 (30.3%) were reported. The frequency of vertigo in headache patients was significant relationship with ageing. Total 31 headache related vertigo patients were divided into two groups (peripheral (n=27), central (n=4)) and proportion of peripheral vertigo has a positive relevance with headache.

**Conclusions:** The clinical relevance of vertigo in headache patients is associated with increasing age spectrum. The proportion of peripheral vertigo was correlated with vertiginous headache groups. The findings of our study may provide direction for potentially useful diagnostic and therapeutic approach to the attack of vertigo such problem in vertiginous headache patients.
SURGICAL TREATMENT FOR PAIN ATTRIBUTED TO A LESION OR DISEASE OF THE TRIGEMINAL NERVE – A SINGLE-CENTER EXPERIENCE

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1Hospital de Cascais Dr. José de Almeida, Department Of Neurology, Alcabideche, Portugal, 2Hospital Professor Doutor Fernando Fonseca, Department Of Neurology, Amadora, Portugal, 3Centro Hospitalar Lisboa Ocidental, Department Of Neurology, Lisbon, Portugal, 4Centro Hospitalar Lisboa Oci
dental, Department Of Neurosurgery, Lisbon, Portugal

Background and Aims:: According to ICHD-3, “Pain attributed to a lesion or disease of the trigeminal nerve” (PLDTN) includes both trigeminal neuralgia (TN) and painful trigeminal neuropathy. Despite initial preference for medical management, patients with refractory pain or intolerant to drug therapy side effects are candidates for surgical therapy. We aimed to characterize a single-center population of patients selected for surgical management of PLDTN, accessing surgery effectiveness and patient satisfaction.

Methods:: Clinical information from patients undergoing surgery for PLDTN between January 2010 and March 2021 at CHLO was reviewed retrospectively. Surgery effectiveness and patient satisfaction was evaluated resorting to the Penn Facial Pain Scale-Revised (PFPSR) and the Patient's Global Impression of Change Scale (PGICS), applied by the telephone.

Results:: Twenty-three patients underwent surgical therapy, with a time from symptom onset to first neurosurgery appointment of 6.43±5.44 years (mean±standard deviation). By the first appointment, patients were medicated with 3±2 drugs for pain control. Most patients had classical TN (73.9%), followed by secondary (8.7%), idiopathic TN (8.7%) and painful post-traumatic trigeminal neuropathy (8.7%). Microvascular decompression (MD) was performed in 65.2%, Gasserian ganglion radiofrequency in 17.4%, partial rhizotomy (PR) in 4.3% and MD+PR in 13.0% of cases respectively. Thirteen patients (56.5%) answered to the telephone survey with an average surgery satisfaction score (PGICS) of 5.77 (1 to 7). Half of these patients became medication free after surgery.

Conclusions:: Surgery for PLDTN is an effective management option that prevents polymedication and pain persistence over the years if earlier referral to Neurosurgery outpatient clinic.
CASE REPORT: ATYPICAL MIGRAINE AS A SENTINEL SYMPTOM FOR SARS-COV2 INFECTION.

Ennio Pucci¹, Marco Quintilio Falvo², Valentina Nava¹, Marta Lagorio¹
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Background and Aims:: Migraine without aura is the most frequent of the forms of migraines (about 60% - 80% of all forms of migraines). There are many causes that can trigger migraines, including infections (IHS ICDH-3).

Methods:: 69 year old woman. Professional nurse. Family history of migraine (maternal line). Arising in school age. Diagnosis made according to the IHS ICDH-3 criteria. The patient presented 2-3 crises / month with pulsating pain in the bilateral frontotemporal region, medium-strong intensity, associated with photo-phonophobia, nausea, sometimes vomiting. Duration 24-36 hours. Triggering factors: menstruation and psychophysical stress. After menopause (49 years) reduction of intensity, duration and frequency with 1-2 crises / month related stress lasting 12-24 hours and responsive to NSAID intake. No preventive therapy performed.

Results:: On 29.11.2020 episode of atypical headache (described as different from other episodes) with very strong, throbbing, stabbing, burning pain in the bilateral frontotemporal region, unresponsive to the intake of NSAIDs. Duration 24 hours. No other symptoms reported, afebrile. 30.11.2020: TNF fast: +. Molecular TNF: positive for SARS COV 2. During the period of infection headache present whenever the patient had fever and was unresponsive to paracetamol.

Conclusions:: In our case report, atypical migraine can be considered a sentinel symptom of an initial infection. The patient works as a professional nurse in the ward which had become Covid on 3.11.2020.
PRIMARY HEADACHES IN A GROUP OF HOSPITAL WORKERS DURING SARS-COV2 INFECTION: AN OBSERVATIONAL STUDY.

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University of Pavia, Department Of Brain And Behavioral Sciences, Pavia, Italy

Background and Aims:: Headaches represent at the same time the symptom and the disease, while the secondary ones are the expression of an ongoing pathology that can be systemic, locoregional or distant. The aim of this study is to determine the prevalence rate in the workplace in a ward (Nucleo Alzheimer) during the period of Sars-COV2 infection. This survey was carried out using 2 questionnaires: 1 (work activity sheet), 2 (headache sheet according to IHS criteria).

Methods:: All health personnel belonging to the Alzheimer Nucleus of the IDR S. Margherita di Pavia were subjected to compilation of questionnaires during the Sars-COV2 infection period.

Results:: From the analysis of the questionnaires administered, it was found that out of 15 workers, 10 were women and 5 were men. 4 (all women had migraines without aura) and 7 tension-type headaches (5 women and 2 men). Before the Sars-COV2 period, only 2 workers had migraine without aura and 2 tension-type headaches (all women). All 11 workers reported stress, insomnia, and concern for family members and their own health. None of the workers at the time of testing had been vaccinated.

Conclusions:: Factors related to the work environment are able to increase the frequency and / or intensity of pre-existing headaches. It is also likely that particular situations can give rise to or cause some forms of headache under certain working conditions. Excessive responsibility or, on the contrary, disaffection and incongruous work rhythms should be considered among the occupational risk factors.
FEATURES OF THE CLINICAL PICTURE OF CERVICOGENIC HEADACHE DEPENDING ON THE LEVEL OF THE VERTEBRAL DAMAGE

Dina Khaibullina, Farida Devlikamova, Yury Maximov, Bulat Gubeev, Daniyar Mansurov, Asya Khaibullina, Yuliya Karpukhina

Background and Aims:: Relevance. About 70% of patients with neck pain simultaneously experience a headache, only in 18% of cases the headache is considered as a consequence of neck pain. Objective: To identify the features of the cervicogenic headache clinic depending on the level of neck damage.

Methods:: 110 patients with complaints of neck pain radiating to the head (mean age 38.7±2.3 years; 68 (61.8%) women and 42 (38.2%) men; symptoms from 20 days till 11 years), were included in the study. The diagnosis of cervicogenic headache was verified according to diagnostic criteria (ICHD-3, 2018).

Results:: 100% of patients had neck pain. Crunching sound which occurs during movement was observed in 28.1%, neck movement limitation – 51.8%, visual disturbances – 60.0%, unilateral noise in the ear-14.5%. Cervicogenic headache associated with changes in C0-Ci-CII was detected in 49 (44.5%) cases and was characterized by unilateral pain (82.7%), visual disturbances, non-systemic vertigo associated with the neck position. Changes in CIII-CIV – in 27 (24.5%) cases were manifested by intense unilateral, throbbing headache with autonomic symptoms. Palpation of CIII-CIV from the headache localization led to clinical manifestations increase. The simultaneous lesion of C0-Ci-CII and CIII-CIV was characterized by unilateral occipital-parietal headache with irradiation to the frontotemporal and ocular region, which had an autonomic disorder, was accompanied by vertigo, nausea, simulating a migraine. CV-CVII do not play a significant role in the cervicogenic headache.

Conclusions:: Thus, the level of localization of cervical spine dysfunction affects the clinical features of cervicogenic headache.
COVID-19 AND HEADACHE: IMPACT ON PRE-EXISTING AND CHARACTERISTICS OF DE NOVO: A CROSS-SECTIONAL STUDY

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Background and Aims:: Background: Headache is a common symptom during and after acute respiratory syndrome coronavirus 2 (SARS-COV-2). Objective: To study headache character in relation to SARS-COV-2 infection.

Methods:: This was a cross-sectional study. Patients who had SARS-COV-2 and presented to the headache clinic within 3 months after the onset of infections were identified to the study. Participants were grouped into categories according to having previous or de novo headache.

Results:: A total of 121 patients were included in this study. Their mean age was 35.29 ±9.54 and most of them were females (83.5%). Prior to SARS-COV-2 infections, 85 (70.2%) had migraine and 18(14.9%) experienced a tension-type headache while 18 (14.9) reported de novo headache post SARS-COV-2. Post SARS-COV-2, the patient had significant increase in headache days 11.09±8.45 compared with 8.66±7.49 headache days before SARS-COV-2 infection (p< 0.006). Post SARS-COV-2 infection, the usage of analgesic increased significantly by the patient with migraine (2.31±1.65 vs 3.05±2.09, p= 0.002) while the patient with tension type headache had statistically significant increase in severity (5.556±1.86 vs 7±2.25, p= 0.033) and frequency (7±6.29 vs 12.72±7.96, p=0.006) of headache attacks.. Patients younger than 40 years had longer duration of the headache attack (18.50±16.44 vs 5.5± 9.07, p=0.045). Male patients compared to females (8.66±1.15 versus 5.93±2.01 p=0.04) had more severe headache.

Conclusions:: Primary headache get worse after SARS-COV-2 infection. De novo primary headache is frequent post SARS-COV-2 infection. Young male patients with SARS-COV-2 infection tend to have worse headache. These features may be helpful in diagnosing the headache related to SARS-COV-2.
USE OF TRADITIONAL MEDICINE IN TREATMENT OF MIGRAINE DURING CORONAVIRUS DISEASE 2019 (COVID-19) PANDEMIC- AN ONLINE SURVEY

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Background and Aims:: Since the emergence of COVID-19 pandemic, patients with migraine were specifically vulnerable to worsening of their headaches, in addition to inadequate quality of medical care and overall psychosocial stressors. Traditional medicine (TM) has been used for centuries to treat headache disorders, and around 2/3 of migraine patients reported seeking TM in literature.

Methods:: We conducted an internet-based, cross-sectional study, to assess the use of TM in treatment of migraine amid COVID-19 pandemic. A self-administered questionnaire was distributed to patients with migraine from the headache clinic in the largest neurology center in Kuwait, and was also posted on several medical social-media accounts.

Results:: A total of 1018 patients completed the survey. TM was used by 406 (39.9%) respondents; 353 (86.9%) females, with mean age of 34 ± 9.5 years, and mean disease-duration of 9.8 ± 8.3 years. The most common reported TM methods were; head-massage by 52.3%, head-banding by 47.9%, herbal-drinks by 45.8%, and essential-oil aromatherapy by 37.2% respondents. Hijama and Farry were reported by 1.1%, and 0.5%, respectively. Higher migraine frequency (p <0.001) and migraine severity (p=0.002), older age (p =0.04), longer disease duration (p =0.005), non-compliance to treatments (p<0.02), and less communication with physicians were associated with higher TM use.

Conclusions:: Worsening of migraine, in addition to the overall negative impact of COVID-19 pandemic, has forced the patients to self-treat themselves by using TM, despite being compliant to their conventional treatments. Neurologists should prepare their patients with "rescue" strategies for headache management, and new means of communication, to face these "new normal" challenges.
IMPACT OF COVID-19 PANDEMIC ON THE CARE OF PATIENTS WITH MIGRAINE

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Background and Aims:: Migraine is one of the most prevalent chronic diseases. The COVID-19 pandemic and the consequent deep remodeling of health care may have contributed to the worsening of migraine. We aim to study the impact of COVID-19 pandemic on the care of patients with migraine.

Methods:: Cross-sectional study with patients with migraine followed in a Neurology outpatient clinic. Patients completed an online survey that included variables related to migraine, treatment and healthcare approachability.

Results:: A total of 97 patients completed the survey, mostly female (92.8%), with a mean age of 43.3 years old, in a full-time job (60.8%), 14.4% changed to teleworking. There was an increasing of anxiety (87.6%) and TV watching (63.9%) and a decrease of exercise (52.6%) and quality of sleep (56.7%). There was a worsening of pain severity in 54.6% patients, with greater need of analgesia (56.7%), 26.8% reported difficulty in getting their medication, botox injections treatment was mostly delayed (82.0%) and 20.6% had to go to emergency ward. Only 11.3% had COVID-19, of those 60.0% had worsening of symptoms. The majority had teleconsultation (55.6%), 42.2% reported that frequency of consultations was not appropriate, and that care was different from presential appointments.

Conclusions:: The COVID-19 pandemic had a negative impact in patients with migraine, there were profound changes in habits and, overall, there was an insufficient health care response to these patients. It is urgent to reorganize health care in order to enhance teleconsultation and promote accessibility to health care.
THE MIGRAINE POSTDROME: THE MISUNDERSTOOD PHASE WITH A SIGNIFICANT IMPACT IN QUALITY OF LIFE

Inês Carvalho, Diogo Damas, Catarina Fernandes, Helena Gens, Isabel Luzeiro
Centro Hospitalar e Universitário de Coimbra, Neurology, Coimbra, Portugal

Background and Aims:: The postdromic phase consists in a set of symptoms occurring once the acute headache has resolved. Its duration varies between several hours and one or more days and it occurs in around 2/3 of the patients. Although it is very common and disabling, the postdromic phase is the least studied and understood phase of the migraine attack. We aimed to determine the prevalence, characterize the clinical presentation and assess the impact of the postdromic phase on daily activities, work activity and quality of life.

Methods:: Sequential patients with migraine according to ICHD-3 were screened about the occurrence of postdromic symptoms and its characteristics using a self-fulfilled questionnaire.

Results:: Of 70 evaluable patients, 94,3% reported at least one nonheadache symptom in the postdromic phase. Postdrome symptoms, in order of frequency, included feeling tired (71,2%), photophobia (62,1%) and having difficulty concentrating (57,6%). 58,5% reported an impact on daily activities and 78,8% in quality of life. Migraine relief medication influenced positively the duration of postdromic phase in 83,1%. The headache frequency was not correlated with the frequency (p=0,83) or duration (p=0,06) of the postdromic phase.

Conclusions:: Nonheadache symptoms are common in the postdromic phase, which contributes significantly to overall disability. Migraine medication positively influences the postdromic phase. In contrast, the frequency of attacks does not influence the occurrence or duration of the postdromic period. Understanding migraine postdrome will improve our knowledge in migraine pathophysiology as well as upgrade our therapeutic approaches.
POOLED ANALYSIS OF SAFETY AND EFFICACY OF FREMANEZUMAB IN DIFFERENT RACIAL AND ETHNIC SUBGROUPS OF PATIENTS WITH MIGRAINE

Larry Charleston Iv1, Joshua Cohen2, Xiaoping Ning2, Verena Ramirez Campos2, Steve Barash2, Tamar Lengil3, Byungkun Kim4

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Background and Aims:: Fremanezumab, a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for migraine prevention in adults. These pooled analyses evaluated the safety and efficacy of fremanezumab in racial/ethnic subgroups.

Methods:: These pooled analyses included data from 3 clinical trials (HALO episodic migraine [EM], HALO chronic migraine [CM], and FOCUS [EM/CM with inadequate response to 2-4 prior preventive classes]), in which patients were randomized to 12 weeks of double-blind treatment with quarterly fremanezumab, monthly fremanezumab, or placebo. These pooled analyses assessed changes from baseline in monthly migraine days (MMD), proportion of patients with 50% or greater reduction in MMD from baseline, and adverse events (AEs) based on patients’ racial/ethnic groups.

Results:: This pooled population included 2,842 patients. Quarterly and monthly fremanezumab provided reductions in MMD and increases in the proportion of patients with 50% or greater reduction in MMD from baseline during 12 weeks versus placebo across White and Non-white racial/ethnic groups (Table). In the quarterly fremanezumab, monthly fremanezumab, and placebo groups, respectively, at least 1 AE was reported by 64%, 62%, and 59% of White patients and 66%, 61%, and 53% of Non-white patients (Black/African American patients, 60%, 58%, and 54%; Asian patients, 64%, 62%, and 44%; Other, 85%, 68%, and 81%). The most commonly-reported AEs across all racial/ethnic groups were injection-site erythema, induration, and pain.

Conclusions:: Treatment with fremanezumab was safe and effective, based on reductions in MMD and increases in ≥50% response rates versus placebo, across White and Non-white racial/ethnic groups, including the Asian subgroup.

Table. Reduction in MMD from Baseline and Proportion of Patients with ≥50% Reduction in MMD During the 12-Week Period by Racial/Ethnic Group

<table>
<thead>
<tr>
<th>Racial/ethnic group</th>
<th>n (%)</th>
<th>MMD, mean</th>
<th>Quarterly fremanezumab</th>
<th>Monthly fremanezumab</th>
<th>Placebo</th>
<th>Quarterly fremanezumab</th>
<th>Monthly fremanezumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>2,378 (83.7)</td>
<td>-2.4</td>
<td>-4.82</td>
<td>-4.5</td>
<td>149 (19)</td>
<td>285 (54)</td>
<td>209 (39)</td>
</tr>
<tr>
<td>Non-white</td>
<td>464 (16.3)</td>
<td>-3.3</td>
<td>-4.8b</td>
<td>-4.5b</td>
<td>33 (21)</td>
<td>53 (34)</td>
<td>50 (34)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>191 (6.8)</td>
<td>-3.9</td>
<td>-4.5</td>
<td>-3.6</td>
<td>21 (11)</td>
<td>25 (41)</td>
<td>20 (34)</td>
</tr>
<tr>
<td>Asian</td>
<td>202 (7.1)</td>
<td>-0.9</td>
<td>-3.3b</td>
<td>-3.0b</td>
<td>9 (14)</td>
<td>22 (33)b</td>
<td>21 (30)</td>
</tr>
<tr>
<td>Other</td>
<td>69 (2.4)</td>
<td>-2.7</td>
<td>-4.6</td>
<td>-5.7</td>
<td>3 (15)</td>
<td>6 (23)</td>
<td>9 (41)</td>
</tr>
</tbody>
</table>

MMD: monthly average number of migraine days.

*P<0.0001 versus placebo.

*P<0.05 versus placebo.
ATYPICAL HORTON’S ARTERITIS WITH OCULOMOTOR NERVES INVOLVEMENT AND ACUTE BRAIN ISCHEMIC LESION: A CASE REPORT

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Padova University Hospital, Department Of Neuroscience, Padova, Italy

Background and Aims:: Background: Oculomotor nerves palsy is a less common complication of giant cell arteritis (GCA) than ischemic optic neuritis, nevertheless it occurs in at least 10% of cases. Other rare complications are cerebrovascular ischemic events, which occur in about 7% of cases. The latter can underlie intra-extracranial vessel stenosis or occlusion, mainly in vertebro-basilar territory, but also an arterial-embolic stroke is possible. Aims: We first report a case of histologically proven GCA in which occurred two rare clinical manifestations, both peripheral oculomotor nerves palsy and acute cerebral ischemic stroke. Besides, PET-MRI compatible with aortitis was found, and arterial-embolic etiology of the stroke was hypothesized.

Methods:: Not applicable

Results:: Case report: A 75-year-old woman presented with headache, horizontal diplopia, and ptosis resulted in bilateral sixth nerve palsy and extrinsic right third nerve deficit. Her blood inflammation markers were moderately high, and brain MRI detected a small right frontal spot with DWI restriction, compatible with acute ischemic lesion, in the absence of other causes. Total-body PET MRI showed high hypermetabolism of the thoracic ascending and descending aorta, consistent with aortic inflammation. Left-temporal artery biopsy was performed, showing a severe inflammatory lympho-monocyte infiltrating pattern, with giant cells and necrosis in the artery wall. High dose of intravenous steroid therapy was started with complete recovery.

Conclusions:: Peripheric oculomotor nerves palsy and ischemic stroke are rare complications of GCA. In the case of increased levels of ESR and CRP and oculomotor abnormalities, Horton arteritis is one of the differential diagnoses to be considered.
IDIOPATHIC HYPERTROPHIC PACHYMENINGITIS, A CASE REPORT.

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Background and Aims:: Idiopathic hypertrophic cranial pachymeningitis (ICHP) is a rare entity characterized by chronic inflammation resulting in the thickening of the dura mater. The first cases of IICHP were related to tuberculosis or syphilis. Other causes are rheumatologic diseases, solid neoplasms or lymphoproliferative processes. After extensive evaluation by neuroimaging, lumbar puncture and serum markers (immunological-infectious-granulomatous) and no cause is founded, it is considered idiopathic in origin. Due to the lack of pathophysiological knowledge (whose hypotésis is possibly inflammatory), the appropriate therapeutic management is still a matter of debate. We describe a case of ICHP and its response to treatment with weekly subcutaneous MTX as described in Ruiz-Sandoval's cases.

Methods:: A 33-year-old man with a history of Gilbert's syndrome. In January 2021, he presented an oppressive headache in the cervical and occipital region that worsens with physical activity, intensity 8/10, extending to the frontal region and back, accompanied by dizziness. Neurological examination was positive for bilateral six cranial nerve palsy and meningismus. the rest was unremarkable. Lumbar punctions are shown in table 1.

<table>
<thead>
<tr>
<th></th>
<th>01.01.21</th>
<th>11.03.21</th>
<th>27.03.21</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>8.0</td>
<td>8.0</td>
<td>7.87</td>
</tr>
<tr>
<td>Glucose -mg/dl</td>
<td>125</td>
<td>83</td>
<td>48</td>
</tr>
<tr>
<td>Proteins mg/dl</td>
<td>1,300</td>
<td>175.4</td>
<td>131.9</td>
</tr>
<tr>
<td>Cels - mm³</td>
<td>400</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Lactate - mmol</td>
<td>0</td>
<td>0</td>
<td>2.0</td>
</tr>
<tr>
<td>Gram</td>
<td>negative</td>
<td>negative</td>
<td>negative</td>
</tr>
</tbody>
</table>

Initial study ---> Steroids treatment ---> MTX SC

Converted angiotensin en CSF (ACE) | Negative
Serum levels of IgG4 | Negative
Serum levels IgG anti-PR3, IgG anti-MPO | Negative
Antinuclear - Antibodies - Immunofluorescence | 1:80 --negative

Results:: Cranial MRI scans were made as follows: -26.06.21
Conclusions:: Patient improvements headache and horizontal diplopia; continues MTX subcutaneous /weekly.
Background and Aims:: Available literature on migraine treatment have shown low persistence to preventive medication. The aim of this study is to describe the persistence of oral preventive treatments in subjects with migraine in Spain and its relationship with healthcare resource use (HRU) and associated costs.

Methods:: Data for this observational retrospective study come from electronic medical records in the BIG-PAC® database (Real Life Data) and include migraine patients ≥18 years who started their first oral preventive medication between 01/01/2016 and 30/06/2018. Patients were followed-up for one year and divided in two groups based on their one-year persistence. Differences between groups in HRU and costs (direct and indirect) were compared using 95% confidence intervals (CI).

Results:: A total of 7,866 migraine patients were analyzed: 80.4% women; mean age 48.2 years (SD=14.8); mean time since diagnosis 3.6 years (SD=1.9) and most frequent comorbidities anxiety (35.9%) and dyslipemia (27.0%). First-administered preventive treatments were antidepressants (46.3%) and antiepileptics (22.1%); median time in first-line treatment was 162 days. The persistent and non-persistent groups included respectively 2,390 (30.4%) and 5,414 (69.4%) patients. In the non-persistent group, the average number of medical visits and days of sick leaves increased by 3 (95% CI: 2.56-3.41) and 2.7 (95% CI: 0.84-4.54) days, compared to persistent patients, what raised total annual cost per patient by 622.1€ (95% CI: 414.9-829.2).

Conclusions:: One-year persistence in patients who initiated oral preventive migraine treatments was low. Persistent patients required a lower use of HRU and sick leaves resulting in reduced annual cost per patient.
VITAMIN PRESCRIPTION PATTERN IN SUDAN: AN EVIDENCE OF SUPPLY INDUCED DEMAND

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Background and Aims:: A growing trend of using vitamins has been documented, yet prescription pattern and reasons for use were not studied. The vitamins industry claims benefit in treating several neurological disorders in the absence of supportive evidence. The aim of this study was to explore the prescription pattern among patients attending neurology clinic.

Methods:: A cross-sectional survey was carried out in Alzaytuna Specialized Hospital, Neurology Department, May 2015 – July 2017. All patients had been assessed and investigated. EMG and Nerve conduction studies were performed to confirm diagnosis of some disorders. Structured assessment tool was used that included: information related to demographic, prescribed vitamin drug name and components, referring doctor’s specialty and the diagnosis.

Results:: A total of 335 patients were included, of which 143 are females. Main prescribers were neurologist (33.4%), Internist (22.7%) and the least were ENT, neurosurgeon and rheumatologist. Half of prescriptions were combinations of “B1, B6, B12” (51%) followed by B12 (23.3%). Vitamins were prescribed for variety of conditions including neurological, orthopedic and systemic disease. The Demyelinating diseases and Stroke/ TIA is accounted for (33%) among neurological conditions, where disc radiculopathy (63%) was the major condition across orthopedic condition. No significant differences were shown when testing association between types of vitamins and referred doctors or conditions.

Conclusions:: Neurologists and orthopedic surgeons induce supply for vitamins without any supportive evidence for cost effectiveness. The practice would increase risk of vitamins toxicity as well as risk opportunities of misdiagnosis. Continuous professional development programs should be designed to address misuse and improve evidence base practice and prescription pattern.
Background and Aims:: Transthyretin amyloidosis (ATTR) is a progressive, systemic, and potentially fatal condition in which misfolded transthyretin proteins form amyloid deposits in muscle and organ tissue. Currently available disease modifying ATTR-related pharmacotherapies generally slow or stop the progression of disease and the benefit of early initiation of treatment has been demonstrated. These analyses examine the relationship between time-to-treatment following symptom onset and long-term patient-reported outcomes (PROs) in patients with ATTR.

Methods:: Several PROs, including Composite Autonomic Symptom Scale, Norfolk Quality of Life—Diabetic Neuropathy questionnaire, and SF-36v2 Health Survey, were administered to 34 patients with ATTR (26 with nervous system involvement) at initial and 12-month assessments in a longitudinal, observational, online survey study. Time-to-treatment was calculated as years between self-reported symptom onset and initiation of ATTR-related pharmacotherapy. The associations between time-to-treatment and PROs at 12 months were examined using correlations, effect sizes for mean differences at yearly cut-points, and linear regression.

Results:: Longer time-to-treatment was at least moderately correlated with autonomic dysfunction including orthostatic hypotension and vasomotor dysfunction, large fiber neuropathy, role limitations due to health problems, and poor health perception (all r>|0.40|). Among the 24 PRO scores examined, effect sizes were at least moderate (all d>0.5) for 17 scores at the 5-year time-to-treatment cut-point. Results from regression models were consistent. Similar patterns were observed when examining only patients with nervous system involvement.

Conclusions:: This analysis provides further support for early initiation of pharmacotherapy for patients with ATTR as vital for preserving health and quality of life.
Background and Aims:: Hereditary transthyretin amyloidosis (hATTR) is a rare, progressive, systemic, fatal condition in which misfolded transthyretin proteins form amyloid in tissues and organs, often manifesting in polyneuropathy (hATTR-PN). The FDA has approved 2 gene-silencing pharmacotherapies for hATTR-PN: inotersen, administered subcutaneously; and patisiran, administered intravenously. Patient satisfaction for each treatment was examined during a period overlapping with the COVID-19 pandemic.

Methods:: Patients with hATTR-PN (with and without accompanying cardiomyopathy) in the United States participated in an observational, online survey between January 1 and October 25, 2020. The Treatment Satisfaction Questionnaire for Medication, version II (TSQMvII), was administered to 29 patients currently being treated with inotersen (n=11) or patisiran (n=18). TSQMvII produces 4 scale scores—Effectiveness, Side Effects, Convenience, and Global Satisfaction—ranging from 0 to 100. Higher scores indicate greater satisfaction. TSQMvII scores were descriptively compared between treatment groups.

Results:: Patients receiving inotersen indicated greater satisfaction with convenience than patients receiving patisiran (mean, 76.3 [SD=19.4] vs 58.6 [15.3], respectively), and less dissatisfaction with treatment side effects (86.1 [16.4] vs 68.3 [19.0]). Ratings were comparable between treatments with respect to effectiveness (72.0 [21.5] vs 67.1 [19.7]) and global satisfaction (78.0 [20.0] vs 74.5 [21.7]).

Conclusions:: While inotersen and patisiran were rated similarly in effectiveness and overall treatment satisfaction, inotersen was associated with less dissatisfaction with side effects and greater convenience, with the latter possibly reflecting differences in mode of administration (ie, at home vs visit to a clinical site), which may be particularly important during a pandemic.
FACTORS ASSOCIATED WITH GREATER HEALTH-RELATED QUALITY OF LIFE BENEFITS IN PEOPLE WITH HATTR AMYLOIDOSIS WITH POLYNEUROPATHY TREATED WITH INOTERSEN

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Background and Aims:: Hereditary transthyretin-mediated amyloidosis with polyneuropathy (hATTR-PN) is a genetic condition that shortens lifespan and carries significant morbidity. We aimed to identify factors associated with greater benefits from inotersen, measured by changes in Norfolk QOL–DN total score (TQOL, score range −4 to 136, higher scores indicating poorer QOL).

Methods:: We used data from the inotersen randomized, double-blind, placebo-controlled phase 2/3 trial for hATTR-PN, NEURO-TTR (NCT01737398, 66 weeks). LASSO regression models predicted TQOL change scores from baseline in the inotersen and placebo arms. Individualized response scores were calculated as differences between predicted change scores had patients received inotersen versus placebo. Patients were ranked by response scores from largest to smallest to define the subpopulation with greatest benefit (top 50%). Unadjusted TQOL change scores of inotersen-treated versus placebo-treated patients were compared within the greatest-benefit subpopulation.

Results:: The overall mean±SD TQOL change was −0.20±19.13 for inotersen (indicating no/minimal change) and 10.77±21.13 for placebo (indicating deterioration). Within people who benefited the most, the mean TQOL change was −11.03±17.06 (improvement) for inotersen and 11.24±22.97 (deterioration) for placebo (P<0.001). Compared with the overall population, patients in the greatest-benefit subpopulation were younger, more likely to have PND scores 1 or 2, less likely to have previous treatment and Thr60Ala, Leu58His, or Ser77Tyr mutations, and a higher (worse) baseline TQOL.

Conclusions:: People with hATTR-PN who were younger and/or at earlier polyneuropathy stages experienced greater HR-QOL benefits from inotersen over 66 weeks. These findings underscore the need for early diagnosis and treatment initiation in hATTR-PN.
HOSPITAL DIRECT COST OF STROKE IN SUB SAHARAN AFRICA: THE CASE OF SENEGAL.

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Background and Aims:: Stroke is a major public health problem because of its frequency, severity and cost. The aim of this study was to estimate the direct cost of care for stroke in hospital for clinical neuroscience of Fann Hospital in Dakar and to identify associated factors.

Methods:: We conducted a prospective economic study based on prevalence, descriptive and analytical. Patients were enrolled from June 1, 2016 to May 31, 2017. Our study population consisted of all patients hospitalized for stroke during the study period.

Results:: A total of 291 patients were included. The average cost was 450717 XOF ± 405214(825$ ± 742). The mean cost of intracerebral hemorrhage was higher 552420 XOF ± 591391(1012$ ± 1083) than that of cerebral infarct 390695 XOF ± 220978 (715$ ± 405) p = 0.07. Paraclinical investigations and hospitalization were the main expense items. The main predictors of cost were the duration of hospitalization (p <0.000001), intensive care unit and NIHSS score (p = 0.00021).

Conclusions:: The cost of stroke is high in Senegal and it is largely supported by patients. Duration of hospitalization and clinical severity are the main factors associated with total cost. Primary prevention must be a priority in our health policy.
SWITCHING MEDICATION WITHIN 12 MONTHS OF INITIATING CALCITONIN GENE-RELATED PEPTIDE MONOCLONAL ANTIBODIES VERSUS OTHER PREVENTIVE TREATMENTS FOR MIGRAINE

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Background and Aims:: Monoclonal antibodies targeting calcitonin gene-related peptide pathway (CGRP mAb) for migraine prevention are FDA-approved. This study assessed 12-month real-world switching patterns for patients initiating CGRP mAb versus other preventive migraine (non-CGRP) treatments.

Methods:: This retrospective, observational study was performed using IBM® MarketScan® Databases. Adults with ≥1 claim (first claim=index) for CGRP mAb (erenumab, fremanezumab, or galcanezumab) or non-CGRP treatments (e.g., antiepileptics, antidepressants, beta-blockers) between 1 May 2018 and 30 June 2019 with continuous enrollment for 12 months pre- and post-index (follow-up) were included. First switch occurred when patients discontinued index treatment (≥60-day gap) and started any other non-index CGRP mAb or non-CGRP treatment(s). Time to switch was calculated as days from index to first switch during follow-up. Descriptive, Chi-square (categorical variables), and Student’s t-test (continuous variables) analyses were conducted.

Results:: Eligible patients on CGRP mAb (N=4,528; female:86.2%) were older than patients on non-CGRP treatments (N=10,897; female:85.1%); mean age was 45.1 versus 41.3 years, respectively (P<.001). Over 12-month follow-up, 59.0% of CGRP mAb and 76.4% of non-CGRP initiators discontinued therapy (P<.001). Of these, 61.9% of CGRP mAb and 27.1% of non-CGRP initiators switched to another non-index CGRP mAb or non-CGRP treatment(s). Time to switch was similar (CGRP mAb: 180.7 days vs. non-CGRP treatments: 177.6 days; P=.15).

Conclusions:: CGRP mAb initiators were less likely to discontinue therapy over the 12-month follow-up period versus non-CGRP initiators. However, of those who discontinued index treatment, CGRP mAb initiators were more likely to switch to another preventive compared with those on non-CGRP treatments.
PATTERN AND OUTCOME OF NEUROCRITICAL DISORDERS IN MULTICENTER HOSPITALS IN KHARTOUM STATE, SUDAN. OCTOBER 2020-JANUARY 2021.

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Background and Aims:: Background Neurocritical care is a growing subspecialty. It concerns with the management of life-threatening neurological disorders. There is limited information regarding epidemiological data, disease characteristics, variability of clinical care, and in-hospital mortality of neurocritical patients worldwide. Objectives To study the pattern and outcome of neurocritical disorders as well as to highlight on neurological consultation in intensive care unit.

Methods:: Methodology This is a prospective observational study which was conducted in neurocritical patients who admitted in four intensive care units of major hospitals in Khartoum state during the period from October 2020 to January 2021.

Results:: Results Seventy two neurocritical patients were included in this study, 40(55.6%) were males and 32(44.4%) were females. 23(31.9%) patients with stroke, 12 (16.7%), with encephalitis, 9 (12.5%) with status epilepticus,6 (8.3%) with Guillain Barre syndrome, 4(5.6%) with MG and 16(22.2%) patients were consulted for neurological manifestation developed within the intensive care unit stay. 23 patients (39.9%) needed MV which was the major indication for intensive care unit admission.21 (29.2%) patients fully recovered,35 (48.6%) partially recovered and 16 (22.2%) died

Conclusions:: Conclusion & Recommendation Stroke was the dominant diagnostic pattern requiring intensive care unit admission. The majority of patients partially recovered. Establishing specialized neurocritical intensive care units with effective collaborations between neurologists, neurosurgeons and intensivists will improve the practice and outcome in this hot field.
THE NEUROLOGICAL EMERGENCIES ADMITTED TO ICU: FREQUENCY, ETIOLOGY AND OUTCOME AT KHARTOUM STATE HOSPITALS IN THE PERIOD FROM OCTOBER 2019 TO APRIL 2020

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Background and Aims: Neurological emergencies are frequent presentations and often times with devastating short and long term consequences. Neurological disorders are increasingly prevalent in Sub-Saharan Africa with paucity of data on adult neurological emergencies in our context. Objective: To study etiologies, patterns of clinical presentation, and outcomes of neurological emergencies patients admitted to ICU

Methods: A Prospective study enrolled 103 patients with neurological emergencies admitted to ICU Khartoum state intensive care departments during the period from October 2019 to April 2020. Data regarding demographics, presentations, clinical examinations, laboratory investigations, indications of ICU admission, diagnosis of neurological conditions, length of ICU stay, patterns of medications and outcomes were collected. Data was analyzed by using SPSS v. 21.0

Results: Among 103 patients, 58(56%) were males and 45(44%) were females, and their mean age was 56.4±16.8 years. Meningitis (n=28; 27.2%), encephalitis (n=28; 27.2%), ischemic stroke (n=19; 18.4%) and hemorrhagic stroke (n=13; 12.6%) were the common diagnosis. Altered mental status was the predominant complain in 66(64.1%) patients. A decreased level of consciousness was the major indication of ICU admission in 77(74.8%) patients. 45(44%) patients improved and discharged, 42(41%) and 16(15%) died ; most due to aspiration pneumonia (n=25; 24.3%).

Conclusions: Sudanese patients with neurological emergencies admitted to ICU were older and mostly males. Meningitis, encephalitis and stroke were the main diagnoses. Patients commonly presented with altered mental status. Half of the patients were improved and aspiration pneumonia observed in a quarter of the patients.
REAL-WORLD IMPACT OF PERAMPanEL USE AMONG PATIENTS DIAGNOSED WITH EPILEPSY IN THE UNITED STATES

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Background and Aims:: Real-world experience with antiepileptic drugs (AEDs) has important repercussions on outcomes and quality of care. Our aim was to evaluate patient experience with perampanel in the USA.

Methods:: A multi-center survey was completed by patients who were ≥18 years old, had a physician confirmed epilepsy diagnosis, used perampanel for ≥4 months, and provided informed consent. Patients provided sociodemographics, treatment history, experiences before perampanel and currently, treatment satisfaction (0-100), medication adherence, quality of life (QoL) and healthcare resource utilization. Statistical analyses were performed using SAS Software, Version 9.4.

Results:: Patients (N=61) were mean age 42.8 years, 63.9% female, 75.4% white and 96.7% had health insurance. Patients had focal onset (62.3%) and primary generalized seizures (45.9%). Mean perampanel exposure was 2.5 years and 62.3% were adherent; 55.7% were taking sodium-channel blockers concomitantly. Patients reported 20.4 (SD=60.0) versus 5.5 (SD=13.2) seizures/month before perampanel and currently, respectively. Compared to prior AEDs, patients “strongly agreed” that perampanel allowed them to live a more normal life (36.1% versus 27.5%) and worked as intended if they missed a dose (16.4% versus 7.8%). Satisfaction scores for perampanel were, 71.8 for effectiveness, 84.0 for convenience and 71.9 for global satisfaction. Perampanel use was associated with improvements in QoL and fewer symptoms of depression and anxiety. Patients had fewer epilepsy-related office (1.8 versus 2.7) and emergency room visits (0.7 versus 2.2) compared to 6 months prior to perampanel initiation.

Conclusions:: Epilepsy patients taking perampanel reported reduced number of seizures, better QoL, lower healthcare resource use and high patient satisfaction in the real-world setting.
Background and Aims:: In June 2019, the Institute celebrated its centenary. The history of scientific activity of the Laboratory of Neuro-Orthopedics and Pain Problems is interesting.

Methods:: The archival materials of the institution were studied.

Results:: In August 1990, 4 scientific associates and 2 doctors from the Kyiv branch of the Kharkiv Research and Scientific Institute of Neurology and Psychiatry were transferred to the Kyiv Research and Scientific Institute of Orthopedics. In May 2006, they established an independent neuro-orthopedic laboratory. Today the Laboratory is expanded and conducts scientific researches in the Institute clinics. Criteria for neurotrophic disorders in patients with chronic hematogenous, traumatic osteomyelitis were developed. A number of degenerative, dystrophic injuries of extremities joints of vertebrogenic origin were revealed. The role of peripheral autonomic nerve structures and spinal cord in pathology formation was established in children with congenital malformations of extremities major joints, both at regional level and in body as a whole. Criteria for diagnostics of pain in vertebral body fractures on background of systemic osteoporosis under deformable spondylosis were revealed. Special features of nervous system disorder in persons with funnel chest deformation were established. The original classification of neuro-orthopedic pain syndromes and neurological complications in patients with amputated extremity parts was developed. The neurological examinations of servicemen of the Armed Forces of Ukraine having received a combat extremity injury within War in Donbass are conducted with further surgical treatment in the Institute clinics.

Conclusions:: The Laboratory of Neuro-Orthopedics and Pain Problems has prospects for further development, working closely with orthopedists, neurologists in Ukraine and abroad.
ATYPICAL MANIFESTATION OF PANCOAST TUMOR WITH NEUROPSYCHOLOGICAL DISORDERS

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Background and Aims: Introduction: Horner’s syndrome was named after Swiss ophthalmologist Johann-Friedrich Horner (1831–1886), who first described it in 1869. The French physiologist Claude Bernard (1813–1878) also took part in the discovery of this particular syndrome, therefore it is also sometimes referred to as Bernhard-Horner Syndrome. It is one of the most known and rare neurological syndromes that can cause a rare clinical manifestation of the also rare Pancoast-type lung cancer. The Pancoast tumor, first described by the British surgeon Edward Selleck Hare (1812–1838) and afterwards by the Italian physician Publio Ciuffini (18??–19??) in 1911, was finally named after the American radiologist Henry Pancoast (1875–1939), and it is a rare and rapidly spreading peripheral tumor of the pulmonary apex.

Methods: Case report: 72-year old patient examined at the Emergency Department due to memory impairment 7 days before.

Results: The results show Horner’s syndrome with pupil contraction, blepharoptosis and left eye enophthalmos, along with impairment of memory abilities, bradypsychia and slowness of movement (bradykinesia). The patient was subjected to chest x-ray and cerebral CT scan, which revealed a tumor at the pulmonary apex and brain metastases respective.

Conclusions: Conclusion: The past discovery of two major syndromes was a case of international collaboration. We must all never omit to show our respect and cite the masters of Medicine, past and contemporary alike. In the context of the Emergency Department, the atypical manifestation of Pancoast tumors with neuropsychological disorders may mislead physicians and result in patients being referred to in outpatient clinics. According to literature, the scientific interest for both these eponymous syndromes remains unchanged throughout the century, with reports published as recent as in 2020.
Background and Aims:: The year 2021 marks the 700th anniversary of medieval poet and philosopher Dante Alighieri death. Dante a giant of Italian literature and credited as “father of the Italian language”, died in 1321 in Ravenna. He had a sound level of medical knowledge, as demonstrated by his description of mental disorders and attended courses at the University of Bologna and at the Sorbonne of Paris, where he may have also studied human anatomy and physiology reading ancient medical writings by Greek, Roman and Arab physicians.

Methods:: Notions of neuroanatomy and neurophysiology (the connection between brain and spinal cord, function of optic nerve and peripheral nerves, knowledge of vegetative nervous system) and descriptions of epileptic seizures and narcolepsy may be found in the Inferno.

Results:: Purgatorio and Paradise demonstrated his imaginative and allegorical travel through all human emotions from Limbic System (Amygdala and hippocampus) to Beatrice smile . “And I, who to the end of all desires/ Was now approaching, even as I ought/The ardour of desire within me ended” (Par. XXXIII, 46-48). The figure of Dante, prophet of hope and witness to the human desire for happiness, can still provide us with words and examples that encourage us on our journey.

Conclusions:: The analysis of neuro-expressionism and Limbic System in Dante’s works confirms that literature and art may be an important source of information and inspiration for neurologists and for history of neurology. Does neurology express art or art express neurology?
ROLE OF THE ALL-UNION INSTITUTE OF EXPERIMENTAL MEDICINE IN THE DEVELOPMENT OF NEUROLOGY IN THE SOVIET RUSSIA

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Background and Aims:: Since 1930, on the initiative of the writer Maxim Gorky, idea of the director of the Leningrad L.N.Fyodorov was being worked out on organization of All-Union Institute for comprehensive study of man. By decree of Council of People's Commissars of the USSR dated October 15, 1932 "On the All-Union Institute of Experimental Medicine in Moscow."

Methods:: We studied Institute's archives and spoke with witnesses and participants of Institute's formation.

Results:: When VIEM was transferred to Moscow, Bach Biochemical Institute formed the VIEM chemistry sector. After the VIEM moved to Moscow, there departments of human physiology (Razenkov), physiology and pathology of sense organs (Stern and Kaplansky), human morphology (Lavrent'ev), biological physical chemistry Rubenstein), organic chemistry (Zelinsky), parasitology E. N. Pavlovsky), viruses (Smorodintsev). At the beginning of 1940s, 3000 people worked at institute, of which 500 were famous scientists and researchers. Institute's annual budget reached 30 million rubles. As of January 1943, structure of Institute consisted of following divisions: Department of Nervous System Physiology (Head - Anokhin) - since 1944 the Institute of Physiology of Soviet Academy of Medical Sciences, laboratory of electrophysiology; laboratory of higher nervous activity; laboratory of neurophysiology; morphological laboratory; Department of General Pathology (Speransky) laboratory of histology, head. - prof. Borovsky; laboratory of experimental pathology, head. - Lebedinskaya; laboratory of infection and immunity, head. - Ostry; laboratory of age physiology and pathology, head. - Arshavsky; chemical laboratory, head. - Saltykov.

Conclusions:: An integrated strategic approach helped organization of fundamental research in neuroscience in Soviet Russia.
NEURO-EXPRESSIONISM IN MICHELANGELO

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Background and Aims:: In addition to being an artistic genius, the Florentine painter, sculptor, and architect Michelangelo Buonarroti (1475–1564) was a master anatomist. He acquired his vast understanding of human anatomy by performing cadaver dissections independently and in an unstructured fashion. Meshberger's assertion that Michelangelo incorporated a view of the brain in the Creation of Adam is compelling and appears to be gaining support among art historians.

Methods:: Michelangelo probably explored gross neuroanatomy.

Results:: He developed an understanding of the human emotions from Limbic System (Amygdala and hippocampus) to Moises Terribilità, pain and maternal love in The Pietà and sublime and beautiful David being regarded as a virtuous fighter for freedom. According to Prof. Semir Zeki the neural activity that correlates with experience of the beautiful is very different from that which correlates with experience of the sublime.

Conclusions:: The analysis of neuro-expressionism and Limbic System in his magnificent beautiful and sublime creations confirms that art may be an important source of inspiration for neurologists.
Background and Aims:: Coronavirus 2019 (COVID-19), with more than 3 million deaths worldwide, is one of the deadliest pandemics in history. Patients with primary mitochondrial diseases (PMDs) are considered at high risk of complications. However, little is known about how COVID-19 affects this group. The aim of our study was to: (1) identify risk factors associated with hospitalisation; and (2) determine outcomes and long-term sequelae of COVID-19 in people with PMDs.

Methods:: Inclusion criteria included: (1) clinico-pathological and/or genetically confirmed PMDs at any age; and (2) COVID-19 infection with compatible symptoms and/or positive PCR testing. Data concerning the underlying diagnosis and COVID-19 infection were anonymously collated by physicians worldwide. The primary outcome was hospitalisation due to COVID-19. Univariable analysis and multivariable-adjusted logistic regression were subsequently applied to data.

Results:: Seventy-two subjects with PMDs from nine countries were included in the study (mean age 41.3 ± 18.2 years); 22 (30.6%) were hospitalised; 43 (59.7%) recovered fully; 25 (34.7%) resolved with sequelae (global deterioration of PMD in six cases, long-COVID-19 in 19 cases); and three (4.2%) died. Statistically significant differences in hospitalisation status were observed for: (1) age (p=0.005); (2) Newcastle Mitochondrial Disease Adult Scale score (p=0.003); (3) modified Rankin scale before COVID-19 (p=0.03); (4) respiratory (p<0.001) and skeletal muscle weakness (p=0.004); (5) wheelchair dependence (p=0.005); and (6) gastrointestinal dysmotility (p=0.002).

Conclusions:: Our study confirms the PMD patients most vulnerable to COVID-19 related hospitalisation, thus helping stratify risk and appropriate management. Long-term sequelae, including worsening of the pre-existing PMD and “long COVID-19 symptoms”, were a frequent finding in our cohort.
NADPH OXIDASE 5: A NEW PLAYER IN PERIPHERAL NEUROPATHY

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Background and Aims:: Peripheral neuropathy (PN) is a debilitating complication affecting over 30% of prediabetic and 60% of type 2 diabetic (T2D) patients. Dyslipidemia has emerged as an independent risk factor for PN. However, the mechanisms by which dyslipidemia leads to nerve injury are not fully defined. While dyslipidemia is associated with systemic and tissue-specific oxidative stress, how it intersects with reactive oxygen species (ROS) sources to contribute to nerve damage is unknown. NADPH oxidase (Nox) enzymes are specialized for ROS production, and of the 7 members, the Nox5 isoform is only expressed in humans. In this study, we examined the role of Nox5 in human nerves and in culture models of PN.

Methods:: Nox5 methylation status, gene and protein expression were assessed in sural nerve biopsies from PN patients. In vitro, human Schwann cell (SC) and neuronal cultures were exposed to the saturated fatty acid palmitate to evaluate Nox5-derived ROS, apoptosis, and Nox4-Nox5 interaction.

Results:: Nox5 promoter was hypomethylated in the sural nerve of patients with worse PN that was associated with increased Nox5 expression. In vitro, palmitate increased Nox5-derived ROS in cultured neurons. Although Nrf2 nuclear translocation was increased after 24 h of palmitate exposure, this effect was not sufficient to reduce upregulated caspase 3 protein expression at early and late time points. Similar results were observed in SCs, with preliminary data of a potential Nox4-Nox5 interaction in palmitate-treated SCs.

Conclusions:: We highlight a role of Nox5 as a target for dyslipidemic oxidative stress that may injure PN-relevant cell types and contribute to PN.
ELECTROMYOGRAPHIC FINDINGS IN PATIENTS WITH LATE-ONSET POMPE DISEASE

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Background and Aims:: Background Pompe disease is an autosomal recessive disorder caused by mutations in the GAA gene encoding the enzyme acid alpha-glucosidase. The late-onset form (LOPD) is characterized by most prominent proximal muscles involvement at four limbs. Electrophysiological study is a diagnostic tool still applied in the diagnostic work up of patients with suspected LOPD. Aim of the study is to evaluate EMG findings including the distribution of involved muscles looking for distal muscle involvement, in a cohort of LOPD patients.

Methods:: 30 LOPD patients (16 M– 14 F) underwent electromyographic evaluation looking at spontaneous activity, MUP analysis and firing rate and recruitment of MUPs in proximal and distal muscles. Moreover electroneurography was performed.

Results:: EMG evidenced the presence of myotonic discharges (MD) in paraspinal muscles in 15/30 patients (50%) but also in distal limb muscles in 5/30 patients (15%). Fibrillation potentials occurred in all muscles where MD were found. Short duration, polyphasic motor unit potentials (MUPs) were found in the paraspinal (35%), proximal (35%) and distal limb muscles (17%) of patients studied. Nerve conduction studies were normal in all patients.

Conclusions:: Conclusion Our results confirmed that myopathic EMG pattern is usually observed in proximal muscles, but we also found a similar pattern in distal muscles revealing a subclinical involvement. Moreover myotonic discharges and denervation activity are present in both paraspinal and distal muscles. We can conclude that it is useful to extend the EMG study also to distal muscles even if not clinically involved.
METFORMIN IMPROVES BIOENERGETICS STATE AND MITOCHONDRIAL DYNAMICS OF DIFFERENT BRAIN REGIONS IN RESTRAINT STRESSED RATS

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Background and Aims:: Mitochondrial dysfunction contribute to ageing and neurodegenerative disorders by producing reactive oxygen species (ROS). Restraint stress as a physical and psychological stressor results in increased generation of ROS, selectively affects the hippocampal neurons that associated with an impairment in spatial learning and memory tasks. Metformin activates AMP-activated protein kinase (AMPK) that presents anti-inflammatory and anti-oxidative properties on the human brain metabolism. Here, we aimed to investigate the adverse effects of restraint stress on the mitochondrial functions of central nervous system which would be attenuated by metformin.

Methods:: Twenty-four male Wistar rats, were randomized into four groups (n = 6), metformin, stress, metformin and stress, and control. Metformin dissolved in distilled water and gavaged once in a day for 14 days. In stress groups rats were immobilized as an acute stress for 6 hours. Rats were then euthanized by decapitation and tricarboxylic acid (TCA) cycle enzyme activity, antioxidant levels, and mitochondrial biogenesis factors were assessed in the frontal, hippocampus, parietal and temporal regions using spectrophotometer and western blot technique.

Results:: Metformin reduced anxiety like behavior, evaluated by elevated plus maze test, caused by restraint stress. There was an increase in activity of TCA cycle enzymes in stress and metformin-stress groups, along with an increase in antioxidant agents, mitochondrial biogenesis factors and dynamic markers.

Conclusions:: Our data suggest mentioned mitochondrial factors increased in the frontal and parietal lobes with metformin pretreatment. Accordingly, metformin can be used as a prophylactic approach against bioenergetics and mitochondrial dysfunction.
MODULATORY POTENTIALS OF VOGLIBOSE ALONG WITH PROBIOTIC IN DIABETIC RATS

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Background and Aims:: Diabetes mellitus regarded as a chronic metabolic disorder characterized by hyperglycemia is prevailing rapidly all over the world and accompanied with various micro and macro vascular complications. The purpose of present study was to examine the modulatory effect of probiotics on different doses of Voglibose in the type 2 diabetic (T2D) rat model.

Methods:: Sprague–Dawley rats (180-250gm) were subjected to high Fat Diet (HFD) for a period of 2 weeks followed by Streptozotocin (STZ) (35mg/kg i.p.) till 21th day of experimental protocol. Then, diabetic rats were treated with Probiotics (75 mg/kg, oral gavage), Voglibose (0.1 mg/kg or 0.3 mg/kg, oral gavage) and combination of different doses of voglibose and probiotics. Serum Lipid parameters such as Total Cholesterol Estimation, Triglyceride estimation and estimation of blood glucose level was done on 0, 14th, 21th and 42th day of the experimental protocol.

Results:: Treatment with Voglibose (0.3mg/kg) and probiotics (75mg/kg) significantly attenuates the body weight (BW) in a dose dependent manner when compared with normal animals. Further, when drugs are given in combination i.e. Voglibose (0.3mg/kg) and probiotics (75mg/kg), significantly decreased the blood glucose level, total cholesterol level in comparison to diabetic group treated with Voglibose (0.3mg/kg). In addition, there is marked increase in the level of high density lipoprotein (HDL) with significant decrease in the level of Low Density lipoprotein (LDL) and very low density lipoprotein (VLDL) level in comparison to diabetic control.

Conclusions:: Thus, it may be concluded that synergistic protective effect on T2D rats may be due to combination of Probiotics and Voglibose.
A YOUNG MALE WITH WALKING DIFFICULTIES AND SUBACUTE BRAINSTEM DYSFUNCTION: ADULT-ONSET LEIGH SYNDROME.

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Background and Aims:: Leigh syndrome (LS) or subacute necrotizing encephalomyelopathy is a progressive, lethal, mitochondrial disease mostly presenting in the childhood.

Methods:: We report a 36 year-old male born in Ivory Coast and living in Italy for the last 20 years. He presented to the Urgency Department after falling over with a 6-month history of progressive dysarthria. When repeatedly asked, he revealed walking difficulties since he was 25 (not investigated) with mute family history. Neurological examination showed: dysarthria, oculomotor limitations for downgaze and convergence, mild right-side paresis with Babinski sign with no reflexes to the lower limbs. A brain magnetic resonance (MRI) showed diffuse white matter lesions restricted to diffusion-weight sequences with no enhancement, localized: around the third ventricle, to the medulla oblongata, and bilaterally at caudate nuclei and putamen. Spectroscopy documented a peak of choline and creatine, increased lactate and reduced n-acetyl-aspartate. Blood and cerebral spinal fluid analyses excluded any autoimmune/demyelinating/infective/paraneoplastic encephalopathy. A quadriceps muscle biopsy showed mild myopathic changes. Mitochondrial genes polymerase-chain-reaction amplification followed by direct sequencing found a 10191T>C variant that is related to LS. Meanwhile the patient worsened his respiratory function and needed a tracheostomy with not-invasive ventilation. He then stabilized in the respiratory rehabilitation, still alive 7 months after diagnosis. Maintenance therapy included: acetylcarnitine 1500 mg, ubidecarenone 50 mg.

Results:: Our patient presented a prolonged history of mild walking difficulties with a subacute onset of brainstem dysfunction that finally resulted LS.

Conclusions:: Only other 9 late-onset cases share the same pathogenic variant 10191T>C
Background and Aims:: Leucoencephalopathies include a broad spectrum of inherited neurodegenerative disorders mainly due to lysosomal or peroxisomal diseases. The involvement of white matter is currently recognized as a common feature of mitochondrial disease. We aimed to determine the clinic-radiological characteristics of mitochondrial leucoencephalopathy (ML) over other types of leucodystrophy.

Methods:: A retrospective study was conducted between 2008 and 2019 including pediatric patients with ML. Detailed analysis of the clinical course and imaging findings was performed. The diagnosis of ML was confirmed through clinical, radiological, biochemical features and sometimes using genetic testing.

Results:: We included 17 patients with ML (M/F = 12/5, mean age: 89.2 ± 49 months). All patients had a disease onset before the age of 2 years (mean age: 12.6 ± 7 months) and most of them had a progressive disease course (76%). Clinical features commonly included encephalopathy (70%), spasticity (70%), gaze abnormalities (53%), and peripheral neuropathy (47%), while epilepsy (23%) and movement disorders (11%) were rarely described. Half of the patients had hyperlactatemia and only 15% had high CSF lactate rate. Brain MRI frequently revealed hypomyelinating leucodystrophy (47%). Other radiological characteristics were white matter cysts (18%), corpus callosum involvement (18%), diffusion restriction (6%), contrast enhancement (6%), basal ganglia and/or brainstem involvement (41%), and lactate peak on spectroscopy (35%). The molecular analysis confirmed a SURF1 mutation in 3 patients and an FBXL4 mutation in one.

Conclusions:: The diagnosis of ML is quite difficult without genetic testing, as clinical presentation often mimics other types of leucodystrophy and biochemical testing does not always help. However, it can be guided through MRI and spectroscopy.
PERIPHERAL NEUROPATHY DUE TO MITOCHONDRIAL DISORDERS IN PEDIATRIC PATIENTS

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Background and Aims:: mitochondrial diseases (MD) constitute a heterogeneous group of disorders that preferentially affect high energy-demanding tissues, as the peripheral nervous system (PNS). The PNS is frequently involved in MD with variable degrees of severity. We aimed to describe the clinical-electric characteristics of peripheral neuropathy (PN) in children with MD.

Methods:: we retrospectively assessed the medical records (clinical and EMG data) of patients diagnosed with MD in our department of child neurology over 11 years. Then, we focused on PN as a clinical feature of MD. In most patients, PN was clinically suspected then confirmed later through EMG. In each patient, we determined the type, severity, and distribution of PN along with the associated signs.

Results:: among the 92 patients with MD, we selected 17 patients (M/F=12/5) having PN (18%). At the onset, the mean age was 24.6±25 months and most patients (47%) had encephalopathy and generalized hypotonia, while 35% had gait abnormalities and 11% had a muscular weakness. At follow-up, besides PN, 82% had a complex neurological presentation, including encephalopathy (85%), hypotonia (85%), spasticity (43%), movement disorders (43%), epilepsy (35%) and ophthalmoplegia (23%). On EMG, 11 patients had a demyelinating polyneuropathy whom genetic study showed a SURF1 and FBXL4 mutation in 2 patients, while only 5 had an axonal polyneuropathy. PN was sensory-motor in 10 patients and pure motor in 5.

Conclusions:: PN is a common feature in MD. Although suspecting the presence of PN in a child with a complex multi-system presentation is challenging, the type of PN can guide the molecular analysis.
CENTRAL PONTINE MYELINOLYSIS IN ACUTE MALNUTRITION: CASE REPORT

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Background and Aims:: Central pontine myelinolysis (CPM) is a rare non-inflammatory neurologic condition most frequently caused by the rapid correction of metabolic disturbances as part of osmotic demyelination syndrome (ODS). It is characterized by damage to regions of the brain, most commonly pontine white matter tracts. Clinical manifestations can appear within several days and can range from encephalopathy to coma and death. CPM has been reported in cases of patients with alcohol use disorder, severe burns, liver transplantation, anorexia nervosa, hyperemesis gravidarum and hyperglycemic or hyponatremic states followed by a rapid correction.

Methods:: We report a 30 year old male patient with 2 week course of progressive weakness that begins in the lower extremities and subsequently involves upper extremities, with subsequent onset of diplopia, dysphagia and dysphonia in whom hydroelectrolyte, glycemic, infectious disorders and chronic alcohol consumption were ruled out. The only related triggering factor is the decrease in protein-calorie intake, marked decrease in weight and BMI 16 in the last few months as a consequence of the current pandemic economic crisis.

Results::
MAGE 1. Brain Magnetic Resonance (T2, T2 FLAIR, Diffusion-weighted imaging/DWI)

**Conclusions:** There are few published cases relating ODS and malnutrition, however it is one of the mechanisms that decrease serum tonicity. Nutrition disorders may be a cause of demyelination of white matter after rapid correction and it is important to keep in mind the possibility of progression to CPM.
A NOVEL MUTATION OF PORPHYRIA VARIEGATE WITH PREDOMINANT PAINFUL SENSORIMOTOR PERIPHERAL NEUROPATHY DISCLOSED BY POST GASTRIC BY-PASS COMPLICATIONS: A CASE REPORT

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Background and Aims:: Porphyrias are a group of rare genetic diseases due to various mostly autosomal dominant mutations causing enzymatic deficiency in heme biosynthesis. As a result, neurotoxic porphyrin precursors and light-sensitizing porphyrins accumulate, while their targets determine the disease symptoms. Porphyria variegate (VP), one of the acute hepatic porphyrias, is caused by a PPOX mutation. During acute crisis triggered by drugs, stressors or fasting, an increase of porphobilinogen (PBG), aminolaevulinic acid (ALA) and porphyrins in urine and stool occur, damaging the autonomous, peripheral and central nervous system. Elimination of precipitating factors, heme-infusions, symptomatic treatment of acute symptoms, sufficient carbohydrate supply constitute the key management. Frequently, the disease remains latent life-long, or minimal symptoms are ignored.

Methods:: This 46-year-old woman presented, some days after a gastric by-bass surgery (RYGB), with severe flaccid tetraparesis and neuropathic pain, initially misdiagnosed to be functional.

Results:: The severe sensorimotor polyneuropathy led to further investigations, disclosing high urinary PBG, ALA and porphyrin levels due to a new PPOX mutation. Retrospectively, the patient had had symptoms typical for VP (especially fragile skin, dark urines) for years prior to surgery. With carbohydrate load, rehabilitation and analgesics, she slowly recovered to full mobility, partial autonomy in her daily life activities, but pain persisted.

Conclusions:: This case documents an exceptional complication after RYGB, but suggests also that a screening for porphyria in patients with cardinal symptoms or a family history of acute porphyria prior to any treatment influencing the diet could prevent porphyria crises and their irreversible adverse consequences.
MELAS SYNDROME, CASE REPORT

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Background and Aims:: MELAS syndrome is a mitochondrial cytopathy, which is characterized by encephalomyopathy, lactic acidosis and ‘stroke like’ episodes, and it is caused by mutations in the mitochondrial DNA. It constitutes a rare multisystemic progressive disorder, with major influence in the muscular and nervous system. Clinical signs and symptoms appear mainly in childhood and adolescence (typically < 40 years old), but can appear at any age.

Methods:: This is a case report of a patient hospitalised in Neurology dept, UHC Mother Teresa.

Results:: The patient E.D is 16 years old when he comes to our attention for an evaluation after some episodes of acute headache, photophobia, decreased vision, and difficulty speaking and repeated seizures. In his medical history it is noted a palatoschisis intervention at the age of 2 and behavioral problems since he was a little child, with mild cognitive impairment. His MRI reveals a left edematous fronto-insular lesion and bilateral occipital lesions, of a similar nature. The patients undergo a biochemistry laboratory analysis and also a muscle biopsy, with conclusive evidence of mitochondriopathy.

Conclusions:: MELAS syndrome is a rare genetic and metabolic disorder, which should have a special diagnostic consideration by clinicians when neuroimaging shows cerebral cortical lesions, which do not follow vascular territories. This case is a classic example of the progression of the disease, with clinical relapses and fluctuant lesions similar to ischemia, in neuroimaging. There isn’t yet a clearly defined consensus for treating patients with MELAS syndrome, but there are recommendations towards a symptomatic approach of treatment.
Background and Aims:: Acute intermittent porphyria (AIP) is a rare and challenging hereditary neurovisceral disease. Peripheral neuropathy is considered the most common neurological manifestation of AIP. Posterior reversible encephalopathy syndrome (PRES) is a clinical and radiological syndrome with bilateral reversible lesions, mostly in parieto-occipital gyri, that is associated with many different conditions, especially severe hypertension. seizures in an acute attack of AIP have been reported, especially if associated with abdominal pain.

Methods:: 17-years old female patient, previously known well, presented with acute onset recurrent attacks of tonic-clonic seizures and high blood pressure. Magnetic resonance imaging (MRI) brain showed a picture of PRES (Figure 1). Three attacks of abdominal pain and vomiting occurred before the onset of seizures over six weeks, with no abnormality detected except mild hypokalemia. Antiepileptic medications and dexamethasone started, CSF analysis was unremarkable. Two weeks later, the patient started to be quadriparetic, hypoventilated with autonomic instability, and mechanically ventilated.
Results:: AIP was suspected, and Watson–Schwartz test was positive (figure 2). Porphobilinogen (PBG) and delta-aminolevulinic acid (ALA) in urine sent out. Her medications were revised and all unsafe medications, especially antiepileptics, were stopped. Moreover, she started on a high carbohydrate diet and other supportive measurements with mild improvement. After high levels of PBG and ALA detections, she started on Hematin, with marked improvement and discharged from ICU.
Conclusions:: AIP should also be considered when seizures and PRES are associated with unexplained abdominal pain. A good prognosis could be achieved when early recognition, supportive and hematin therapy, and withdrawal of precipitating factors, including some antiepileptic drugs.
NEUROLOGICAL DISORDERS DUE TO VITAMIN B12 DEFICIENCY

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Background and Aims:: Cobalmins and folate are two vitamins essential for the integrity of the nervous system. Neuropsychiatric disorders are also classic even in the absence of anemia or macrocytosis. The objective of our study is to describe clinical, and evolutionary profile of patients with neurological disorders due to vitamin B12 deficiency.

Methods:: We conducted a retrospective study at neurology department in Sfax over a period of 15 years [2005 - 2020]. We included all patients with neurological manifestations suggestive of vitamin B12 deficiency. We excluded those for whom another associated cause could explain the neurological symptoms.

Results:: We recruited 51 patients (30 men, 21 women). The mean age of onset of the disorder was 53.3 years. The clinical signs of onset were dominated by paresthesias and gait disturbances. Neurological examination showed a posterior cord syndrome in 84.31% associated with pyramidal syndrome in 62.8%. Cerebellar syndrome was found in 21.56%, sphincter disorders 37.25% and polyneuropathy were also found in 62.74% of our patients. Biologically, anemia was observed in 80.3% patients. Macrocytosis was noted in 82.35%. The serum vitamin B12 level was most often decreased. The spinal cord MRI showed a T2 hyperintensities localized in the dorsal region in 9.8%. Brain MRI was normal in the majority of patients. All patients were receiving vitamin B12 treatment. Clinical and biological improvement was noted in most of our patients.

Conclusions:: Vitamin B12 deficiency should kept in mind face of any unexplained progressive neurological symptoms. Early diagnosis and rapid supplementation prevent irreversible damage.
MITOCHONDRIAL NEURO-GASTRO-INTESTINAL ENCEPHALOMYOPATHY: A CASE REPORT

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Background and Aims:: The gastrointestinal symptoms are possible complication in neurological diseases and sometimes the first manifestation of rare genetic diseases as mitochondrial neurogastrointestinal encephalopathy (MNGIE). This association is misdiagnosed by physician without an expertise in rare diseases.

Methods:: A Thirty-two years old woman was evaluated from the juvenile age exclusively in several Gastroenterology Divisions for a severe weight loss due to unexplained malabsorption syndrome. The various histological and endoscopic investigations had never given contributory results. The patient was even diagnosed with Anorexia Nervosa. Furthermore, due to several vomiting episodes, she developed recurrent aspiration pneumonia and she needed intensive care. However her clinical picture was characterized by some neurological signs that had been neglected.

Results:: Neurological examination showed waddling gait, bilateral ptosis with ophthalmoplegia, dysphagia for liquids, proximal weakness of the lower limbs and diffuse muscle atrophy. Brain MRI showed severe bilateral confluent leukoencephalopathy with cortical and subcortical white matter alterations (Fig.1). Electrophysiological study identified an axonal sensory polyneuropathy with normal electromyography (Fig.2). Muscle biopsy showed several fibers with oxidative metabolism deficiency (Fig.3). Considering the combination of neurological features, mitochondrial alterations on muscle biopsy and gastrointestinal impairment, we suspected the mitochondrial neurogastrointestinal encephalopathy (MNGIE). Finally genetic analysis identified the homozygous c.1160-1G>A mutation on the TYMP gene. A few months later, the patient received a liver transplantation but she died as a result of post-surgical complications.
Conclusions:: Neurogenetic diseases are often multisystemic and however misdiagnosed. Our case demonstrates the fundamental role of the multidisciplinary approach to avoid dangerous diagnostic delays.

Fig.2 Electrophysiological study

Fig.3 Muscle Biopsy
VALIDATION OF DIRECT AMP KINASE (AMPK) ACTIVATION FOR TREATMENT OF X-LINKED ADRENOLEUKODYSTROPHY

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Background and Aims:: X-linked Adrenoleukodystrophy (ALD and adrenomyeloneuropathy - AMN) is a neurologic peroxisomal disorder, caused by ABCD1-gene mutations, leading to Very Long Chain Fatty Acid (VLCFA; C26:0) accumulation, AMPK downregulation, inflammation, mitochondrial impairment and demyelination. We investigated PXL770, a clinical-stage new direct AMPK activator, in AMN/ALD models.

Methods:: AMN/ALD patient-derived fibroblasts/lymphocytes and ABCD1-KO mouse glial cells were exposed to PXL770 for 7 days. Phospho-AMPK was measured by Western-blot, VLCFA content by LC-MS, selected gene expression by RT-qPCR and oxygen consumption with a Seahorse Analyzer. PXL770 (oral 75mg/kg, BID, 12 weeks) was administered to ABCD1-KO mice. VLCFA content was measured by LC-MS, sciatic nerve axonal morphology by electronic microscopy, and locomotor function by beam balance test.

Results:: In AMN fibroblasts PXL770 reduced C26:0 levels (-90%, p=0.0001), increased compensatory ABCD2 mRNA levels (9-fold), and improved mitochondrial function by increasing basal and ATP-linked respiration (14% and 112%, respectively) and decreasing proton leak (-25%). Similar profile was achieved in ALD fibroblasts, ALD/AMN lymphocytes and ABCD1-KO mice glial cells. In ALD lymphocytes, PXL770 decreased mRNAs encoding pro-inflammatory proteins including NF-κB, iNOS and CCR3 (2.9-fold, 8.2-fold, 5.9-fold, respectively). In ABCD1-KO mice treated with PXL770, C26:0 levels were decreased in the spinal cord by 29% (greater VLCFA decrease was also observed in brain/plasma). Sciatic nerve axons showed less myelin invaginations (-61%) and neurologic function was improved compared to untreated mice.

Conclusions:: We established preclinical validation for the potential utility of direct AMPK activators as a treatment for X-ALD, supporting further development of PXL770 for this debilitating neurometabolic disease.
MOTOR NEURON DISEASE AS AN OUTCOME OF NEURODEGENERATION, NEUROINFLAMMATION OR MERCURY POISONING?

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Background and Aims:: Amyotrophic lateral sclerosis (ALS) is the main disease in the group of motor neuron diseases. It is fatal disease that affects lateral columns of spinal cord, leads to generalized muscular atrophy. Most severe damage to respiratory muscles resulting from degeneration of motor neurons ultimately leads to certain death approximately 5 months after first symptoms onset. Mercury intoxication (MI) in some cases makes significant contribution to neurodegenerative processes or aggravates existing symptoms of ALS and simultaneously immune deficience.

Methods:: We studied immune status in 29 ALS patients, both genders from 45 to 67 years old and in 139 healthy donors by the same ages, including determination of number of indicators of cellular and humoral immunity, including calculation of immunocompetent cells of T and B-lymphocytes, indicators of phagocytosis of latex particles by leukocytes, pro-inflammatory cytokines IL-2 and IL-6 and immunoglobulins A, M and G. Neurodegenerative changes in brain were studied in transgenic mice with superoxide dismutase defect. Effect of mercury vapor on course of neurodegenerative processes was studied using this experimental model, which also showed signs of severe immunodeficiency.

Results:: We found that 67% of patients with ALS in region of Republic of Mordovia had occupational MI for long period, demonstrated a profound immunodeficiency: decrease of T and B-cells, Ig G and IgA, increase of IgM, IL-2 and IL-6. Revealed deficit of DNA-binding protein of TDP-4 in brains of experimental models. Mice exposed to MI demonstrated more considerable neurodegenerative changes.

Conclusions:: It is difficult to establish which role is primary: neuroinflammation or MI in ALS neurobiology.
BRADYKINESIA IN AMYOTROPHIC LATERAL SCLEROSIS

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Background and Aims:: Amyotrophic lateral sclerosis is primarily characterized by the degeneration of motor neurons, leading to muscle weakness and motor impairment. There are some clinical reports of bradykinesia in this condition, but no studies have objectively assessed voluntary movements in these patients. The relationship between motor neurons involvement and movement abnormalities is also unknown. We here kinematically assessed repetitive finger movements in patients with amyotrophic lateral sclerosis as compared to healthy controls. We investigated possible relationships between altered movement kinematics and neurophysiological measures of motor neurons involvement in patients.

Methods:: Fourteen amyotrophic lateral sclerosis patients and seventy-nine healthy controls were enrolled. Finger tapping was assessed by a motion analysis system. Patients also underwent a motor nerve conduction study, a central motor conduction time assessment, and a needle electromyography. Kinematic data from the two groups were compared by non-parametric tests. Possible relationships between clinical, kinematic and neurophysiological data were assessed in patients.

Results:: Patients performed repetitive finger movements slower than healthy controls. Patients also showed altered movement rhythm during the motor task. Notably, movement slowness in patients correlated with muscle strength, as well as with the amplitude of the compound muscle action potential recorded after nerve stimulation of the muscles involved in the task. Finally, movement slowness correlated with denervation activity. No correlations were found between movement slowness, measures of upper motoneuron involvement, and other clinical and neurophysiological data.

Conclusions:: This study provides a demonstration of movement abnormalities in patients with amyotrophic lateral sclerosis and highlights the pathophysiological role of motoneurons in generating bradykinesia in this condition.
DUX4 EXPRESSION IS INCREASED IN LYMPHOMONOCYTES OF PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS: POSSIBLE INVOLVEMENT IN TDP-43 AGGREGATION?

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Background and Aims:: TAR DNA binding protein-43 (TDP-43) is the main component of cytoplasmic aggregates in motor neurons of Amyotrophic Lateral Sclerosis (ALS) patients. TDP-43 aggregates have also been found in muscle cells of patients with Facioscapulohumeral dystrophy (FSHD), a disease caused by the aberrant expression of DUX4 protein. Interestingly, the expression of DUX4 has been demonstrated to induce TDP-43 aggregation in human FSHD myoblasts and healthy cells transfected with DUX4. Based on these premises, we decided to verify if DUX4 is expressed in cells of ALS patients and, if expressed, its possible involvement in TDP-43 aggregation.

Methods:: Gene and protein expression of DUX4 was assessed by qRT-PCR, Western blot and immunofluorescence in peripheral blood mononuclear cells (PBMCs) obtained from 58 ALS patients and 39 healthy controls.

Results:: While a mild DUX4 protein expression was detected in control PBMCs, a 3-fold increase (p<0.0001) of DUX4 protein levels and a mis-localization in the perinuclear area were observed in ALS PBMCs. Similar results were obtained for DUX4 mRNA levels, measured in a subgroup of subjects. We also confirmed an increased TDP-43 protein expression in ALS PBMCs and identified a positive correlation with DUX4 (r=0.6, p<0.0001). A DUX4/TDP-43 co-localization in the perinuclear region and a tendency to aggregate emerged in a subset of ALS PBMCs underwent immunofluorescence analyses. Finally we demonstrated in an in vitro model that DUX4 upregulation induced an increase of TDP-43 insoluble fraction.

Conclusions:: These results suggest a possible role of DUX4 in TDP-43 aggregation, although further studies are needed.
IMPAIRED RECOGNITION OF DISGUST IN AMYOTROPHIC LATERAL SCLEROSIS IS RELATED TO BASAL GANGLIA INVOLVEMENT

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Background and Aims:: To investigate emotion recognition in amyotrophic lateral sclerosis (ALS) patients without cognitive/behavioural deficits and its relationship with the integrity of basal ganglia, hippocampus and amygdala.

Methods:: Twenty ALS patients without cognitive/behavioural deficits and 52 matched healthy controls performed a neuropsychological assessment including the Comprehensive Affect Testing System (CATS) investigating emotion recognition. All participants underwent also a 3T brain MRI. Volumes of the caudate nucleus, putamen, pallidum, nucleus accumbens, thalamus, amygdala and hippocampus bilaterally were obtained using FIRST in FSL. Sociodemographic, cognitive and MRI data were compared between groups. In ALS patients, correlations between CATS significant findings, brain volumes, cognition, mood and behaviour were explored.

Results:: ALS patients showed altered performances at the CATS total score and at the CATS affect selection and affect matching subtests compared with healthy controls. Among the investigated emotions, patients were significantly less able to recognize disgust compared with controls. No brain volumetric differences were observed between groups. In ALS patients, a lower performance in disgust recognition was related with a lower performance on the Edinburgh Cognitive and Behavioural ALS Screen (ECAS) and reduced volume of the left pallidum.

Conclusions:: Cognitively and behaviourally unimpaired ALS patients showed impaired disgust recognition, which was associated with the degree of basal ganglia pathology. The association with cognitive alterations may suggest impaired disgust recognition as an early marker of cognitive decline. Funding: Italian Ministry of Health (GR-2013-02357415); European Research Council (StG-2016_714388_NeuroTRACK).
CLINICAL AND HORMONAL CHARACTERISTICS OF SPINAL AND BULBAR MUSCULAR ATROPHY (SBMA): A NATION-WIDE STUDY OF 82 KOREAN PATIENTS

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Background and Aims:: Spinal and bulbar muscular atrophy (SBMA) is an X-linked motor neuron disease caused by the expansion of a CAG repeat in the androgen receptor (AR) gene. The aim of this study was to characterize the clinical and genetic features of SBMA in South Korea.

Methods:: 82 genetically confirmed SBMA patients were enrolled. The clinical parameters included were age of onset, disease duration, initial symptom at onset, amyotrophic lateral sclerosis functional rating scale, revised (ALSFRS-R), 6 minute walk test and medical research council sum score (MRCSS) were assessed. The laboratory parameters included were testosterone, luteining hormone, follicle stimulating hormone and creatine kinase.

Results:: A total of 82 patients with SBMA were included in this study. The mean age was 54.87 ± 10.16 years. The mean age of initial symptom was 44.38 ± 9.92 years. The mean number of CAG repeats in the AR gene was 46.4 ± 4.38. Average creatinine kinase level was 967.63 IU/L. 60 out of 81 patients (73.2%) were of lower limb onset. There was a statistically significant correlation between the number of CAG repeats and the age at onset. Interestingly, testosterone levels showed positive correlation with ALSFRS-R score (r=0.273, p=0.014).

Conclusions:: Thw novelty of this study is that we identified clinical features with hormonal levels in characterizing Korean SBMA patients. Longitudinal studies are warranted to understand the natural history of Korean SBMA leading to a better understanding of the disease.
TEMPORAL MUSCLE THICKNESS AS PREDICTOR OF SURVIVAL IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS.

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Background and Aims:: Temporal muscle thickness (TMT), is a new potential Magnetic Resonance Imaging (MRI) biomarker which has shown prognostic relevance in patients with brain metastasis and in some neurological disorders. We aim to investigate the potential clinical value of TMT in patients with Amyotrophic Lateral Sclerosis (ALS)

Methods:: We retrospectively enrolled ALS patients whose clinical, MRI and Electrodiagnostic (EDX) data were available. TMT was calculated on T1-weighted MR images and patients were divided in two cohorts according the median value of TMT. A survival analysis among the two groups was calculated with Kaplan Meier method. The differences of clinical characteristics and EDX parameters between the two groups were calculated with T-Student test for continuous parameters and Chi-Square test for nominal parameters.

Results:: A total of 40 patients were included for the analysis: twenty-six males (65%) and fourteen females (35%) (median age 62 +/- 13y-o, median duration disease 50 +/- 10 months), 11 with upper motor neuron predominance (UMNP) 20 with lower motor neuron predominance (LMNP), 9 with non clinical defined predominance (NCDP). Median TMT value was equal to 6,8 mm. The only parameter that resulted significantly different in the two cohort was the compound motor action potential (CAMP) (p-value: 0,036). TMT, finally, was significantly correlated with overall survival (OS) (lower TMT: median OS 35 +/- 8,0 months, versus higher TMT: median OS 65 +/- 5,1 months, p-value: 0,033).

Conclusions:: This novel and simply MRI marker seems to be a promising surrogate biomarker of sarcopenia and survival in ALS. Our study deserves further investigations in multicenter and prospective trials.
"MENTAL" COMPONENT OF FATIGUE CORRELATES WITH COGNITIVE AND BEHAVIORAL IMPAIRMENT IN AMYOTROPHIC LATERAL SCLEROSIS

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Background and Aims:: Amyotrophic lateral sclerosis (ALS) is increasingly recognized as a multisystem neurogenerative disease, mainly affecting motor neurons, although also characterized by cognitive and behavioral impairment. Fatigue is a symptom of exhaustion unexplained by drug effects, or psychiatric disorders, associated with other fatigue-related symptoms, such as reversible motor weakness and whole-body tiredness, which are only partially relieved by rest. We aim at investigating the clinical correlations between both “physical” and “mental” components of fatigue, measured by the Multidimensional Fatigue Inventory (MFI) scale, and motor and cognitive/behavioral disability in ALS. Moreover, we investigated the correlations between these symptoms and brain resting state functional magnetic resonance imaging (RS-fMRI) alterations in a cohort of patients with ALS.

Methods:: 130 ALS patients were assessed for: motor disability (ALS Functional Rating Scale-Revised, ALFRS-R); cognitive and behavioral dysfunctions (Edinburgh Cognitive and Behavioral ALS Screen, ECAS); fatigue (MFI); anxiety; apathy and daytime sleepiness. Moreover, the collected clinical parameters were correlated with RS-fMRI connectivity changes in 30 ALS patients who underwent MRI.

Results:: Multivariate correlation analysis revealed that “mental” fatigue was positively related to memory and executive dysfunctions. RS-fMRI analysis showed inverse correlations between functional connectivity in the right and left insula (“salience” network) and in the left middle temporal gyrus (Default Mode Network) and mental fatigue.

Conclusions:: Although the “physical” component of fatigue may be influenced by the disease itself, in ALS the “mental” component of fatigue correlates with cognitive and behavioral impairment, as well as with alterations of functional connectivity in extra-motor areas.
RESTING STATE FMRI CORRELATES OF PSEUDOBULBAR SYNDROME IN AMYOTROPHIC LATERAL SCLEROSIS (ALS)

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Background and Aims:: Pseudobulbar syndrome (PBS), referring to exaggerated or inappropriate episodes of laughing and/or crying without an apparent motivating stimulus, has been mainly attributed to bilateral degeneration of corticobulbar tracts. Our objective was to explore brain functional connectivity (FC) correlates of PBS in patients with amyotrophic lateral sclerosis (ALS), the most common motor neuron disease frequently associated to PBS, assessed by Center for Neurologic Study Lability Scale.

Methods:: Resting state functional MRI (RS-fMRI), and voxel-based morphometry (VBM) analyses were performed in 27 ALS patients (13 with PBS; 14 without PBS) and 26 healthy controls (HCs), for investigating functional and structural abnormalities in ALS patients compared to HCs and in patients with PBS compared to patients without PBS.

Results:: Between-patients analysis revealed: decreased FC in the right middle temporal gyrus (MTG), right precuneus and posterior cingulate cortex and an increased FC in the left MTG (default mode network); increased FC in bilateral precuneus (frontoparietal network), right precentral gyrus (sensory-motor network), right insula (salience network); and no significant differences in gray matter atrophy in patients with PBS compared to patients without PBS. Pseudobulbar index was inversely related to FC in the right MTG and positively related to FC in bilateral precuneus, right postcentral gyrus, right insula and anterior cingulate cortex.

Conclusions:: Our findings suggested that alterations of fronto-temporal circuits may be related to PBS in ALS. In particular, decreased FC in the right MTG and increased FC in bilateral precuneus and in right fronto-temporo-parietal areas may underlay PBS in patients with ALS.
LONELINESS IS A THREAT TO NEUROBEHAVIORAL FUNCTIONING IN AMYOTROPHIC LATERAL SCLEROSIS

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Background and Aims:: Perceived social isolation, also termed loneliness, impacts on neurobiological architecture, ensuing significant consequences on mental and physical health. In this framework, we look for a possible negative backlash of loneliness in amyotrophic lateral sclerosis (ALS), a neurodegenerative disease that primarily affects the motor system, but also cognition and behaviour.

Methods:: Cognitive performances, mood, alexithymia, behavioural change and quality of life (QoL) were assessed in 139 consecutive ALS patients. Perceived social isolation was esteemed with the revised UCLA 3-items loneliness scale. Spearman rho correlations (Bonferroni correction, p≤0.003) and the Kruskal-Wallis H tests examined factors associated with UCLA scores. Loneliness, age and disease stage were used as dependent variables in logistic regression, with bootstrap validation, to predict the occurrence of behavioural impairment, mood disorder, and alexithymia.

Results:: The UCLA scores were significantly associated with behavioural changes, mood, alexithymia and QoL, and not with motor functional status, disease duration or cognitive abilities. Having feeling of loneliness (UCLA scores ≥ 4) significantly increased the odds of behavioural impairment, depression and alexithymia by 3, 7 and 5 times respectively.

Conclusions:: In our cohort of ALS patients, the satisfaction of social environment is associated with a sense of life well-being that is not limited to the functional motor status. Our findings indicate that loneliness acts as a threat to neurobehavioral functioning in ALS, as other risk factors do (e.g. advanced disease stages), with potential great impact on patients’ care and clinical trial design.
SERUM CHI3L1 IN AMYOTROPHIC LATERAL SCLEROSIS: A USEFUL TOOL FOR PROGNOSTIC DEFINITION?

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Background and Aims: Neuroinflammation is a key pathophysiological hallmark in amyotrophic lateral sclerosis (ALS), which seems to be linked to the disease progression. Cerebrospinal fluid (CSF) chitinase-3-like protein 1 (CHI3L1), a marker of glial activation, is a recent candidate biomarker of ALS, but less is clear about its value in the serum. In this study, we explore if serum CHI3L1 could add prognostic value as biomarker of ALS.

Methods: CHI3L1 levels were measured by immunoassay kit (Protein SimpleTM) in CSF and serum of ALS patients (n=64) and healthy controls (HC) (n=10). CSF and serum levels were correlated with several clinical parameters, classifying slow and fast ALS progressors according with ALSFRSr slope (lower than the 25th percentile and higher than the 75th percentile, respectively, in our reference population). Between-group comparisons were drawn by Mann-Whitney test and ROC analysis was performed to assess diagnostic performance.

Results:

In CSF CHI3L1 levels were similar in ALS and HC (p=0.97, p=0.98), while in serum CHI3L1 levels were
not significantly different (p=0.43, p=0.45, respectively). Serum CHIT3L1 levels strongly correlated with the disease progression rate (p=0.01, p=0.0085) while no significance was found for CSF (p=0.26, p=0.30). ROC analysis showed that serum CHI3L1 could discriminate between fast and slow ALS progressors (AUC=0.86), while CSF had worse performance (AUC=0.72).

**Conclusions:** Serum CHIT3L1 is significantly elevated in ALS fast progressors, with discriminatory power towards a slower phenotype. Its prognostic role is not confirmed for CSF levels. Our data encourage the research on neuroinflammatory markers in patient stratification as surrogate markers of ALS progression.
Background and Aims:: Mutations in the tropomyosin-receptor kinase fused gene (TFG) are prominently described in Asian countries in association with hereditary motor sensory neuropathy with proximal involvement (HMSN-P), Charcot–Marie–Tooth disease type 2 (CMT2) and hereditary spastic paraplegia type 57 (SPG57). HMSN-P is a rare autosomal dominant motor and sensory neuropathy starting with fasciculations and proximal weakness and progressing slowly with a pattern similar to Amyotrophic Lateral Sclerosis (ALS).

Methods:: Review of the patient's and her relatives' medical history.

Results:: An Italian 30-year-old woman presented with isolated fasciculations, followed four years later by cramps and slowly progressive proximal lower limbs weakness. She had a family history of atypical slowly progressive motor neuron disease in the three previous generations. Neurophysiological studies showed a sensitive axonal neuropathy with diffuse chronic neurogenic sufferance in absence of active denervation except for mild fasciculations. An extensive next-generation sequencing (NGS) panel, including genes associated with diseases affecting the motor neurons, displayed the heterozygous TFG p.Pro285Leu variant, currently described in HMSN-P cases confined to the Far and Middle East. Thus, we considered the mutation found could explain our patient's and her relatives' symptoms, indeed suggestive for HMSN-P, and the pattern of transmission. To the best of our knowledge, this case is the first report of HMSN-P associated with the p.Pro285Leu substitution in a Caucasian patient.

Conclusions:: Inclusion of TFG in worldwide NGS panels could help define atypical familial cases of motor neuron diseases or neuropathies and plan follow-up according to the expected disease course.
VALIDATION OF THE ITALIAN VERSION OF THE RASCH-BUILT OVERALL AMYOTROPHIC LATERAL SCLEROSIS DISABILITY SCALE (ROADS).

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Background and Aims:: The ALS functional rating scale – revised (ALSFRS-R) is widely used for the assessment of ALS patients. Despite its usefulness as a multidimensional scale, the combined score derived from different domains is not linearly related to symptom severity. The Rasch-Built Overall ALS Disability Scale (ROADS), which is linearly weighted and unidimensional, was developed to overcome some of these limitations. Our objectives are to validate the Italian version of the ROADS scale and assess the reliability of its administration to patients versus their caregivers and the correlation to ALSFRS-R.

Methods:: The ROADS questionnaire was administered with the ALSFRS-R to 55 ALS patients and their caregivers during assessments in the Turin ALS Centre. Correlation analysis was performed using Spearman's rho, Bland-Altman difference plots, Cronbach's alpha coefficient and Intraclass Correlation Coefficient; a value of p <0.05 (two-tailed) was considered significant.

Results:: The median normalized ROADS values did not differ significantly between patients and caregivers (73.0, IQR 60.0-86.0 vs 70.0, IQR 57.0-82.0, p=0.524). Their correlation coefficient was high (ICC 0.95, p<0.00; Cronbach’s alpha coefficient 0.94) and the total score agreement based on Bland-Altman showed no systematic directional bias (mean difference: 0.82, 95% limits of agreement: -15.9-17.6). High ICC values were observed when stratifying for sex, age classes and caregiver type. A high correlation was found between ROADS and ALSFRS-R total score (patients’ and caregivers’ correlation coefficients respectively 0.88 and 0.87).

Conclusions:: The ROADS scale is a valid and reliable tool to monitor disease burden, showing a high level of agreement between patients’ and caregivers’ responses.
6MWT AS MEASURE OF MOTOR FUNCTION AND ENDURANCE IN SMA TYPE 3 PATIENTS TREATED WITH NUSINERSEN

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Background and Aims:: Spinal muscular atrophy (SMA) is an autosomal-recessive motor neuron disease causing progressive muscular atrophy and weakness. Nusinersen, an antisense oligonucleotide able to increase functional SMN protein modifying the SMN2 pre-mRNA splicing, is proved to be able to significantly modify the natural course SMA type 1 (the severe phenotype) in infants. Data of efficacy in adults are limited. We aim to investigate the impact of nusinersen therapy in walking resistance in SMA 3 patients since abnormal muscle fatigability represents an additional dimension of attenuated motor function in SMA.

Methods:: From a large Italian cohort of patients we selected 58 ambulant adult SMA3 patients being treated with nusinersen and we analyzed data on 6 minute walking test (6MWT) since baseline (beginning of treatment) to 14 months.

Results:: The 58 patients started therapy at an average age of 40,7 years (18-65 years) and reached
different time points follow up: 25 patients 14 months, 13 patients 10 months, 13 patients 6 months and 7 patients the baseline. Of 46 subjects, the meters walked every single minute during the 6MWT were also collected. We found that there is an increase in the meters walked, cumulative over time which is, compared to the baseline, respectively of 13,2 ± 28 m after 6 months, 20,7±34 m after 10 months and 35 ± 56,8 m after 14 months. 
**Conclusions:** Our data broaden the evidence of nusinersen efficacy in adult ambulant SMA patients. Furthermore, the 6MWT data provide an estimate not only of motor ability, but also of resistance to physical exercise.
E-HEALTH SOLUTIONS FOR AMYOTROPHIC LATERAL SCLEROSIS PATIENTS: A CHATBOT FOR DIETARY MONITORING

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Background and Aims:: Nutritional status is one of the most relevant prognostic factors in Amyotrophic Lateral Sclerosis (ALS), and close monitoring can help avoid severe weight loss over the disease course. We aimed to describe the impact of a technological chatbot on improving the communications between healthcare providers and patients and caregivers for dietary monitoring.

Methods:: We developed a chatbot that provides patients a tool to register their meals through a simple and carefully designed conversational interface. Patients recorded dietary intake three times a week, and they received a nutrition recommendation biweekly. Of these, we monitored body mass index (BMI), caloric intake, need for artificial supplementation and/or thickeners, and ALSFRS-R.

Results:: A total of 26 patients were enrolled and monitored for six months, for a total of 554 fillings (mean of 21/patient). From the recorded data, it appears that patients, on average, ate ¾ of recommended portion, and 66% maintained the caloric intake during the six-month follow-up. The mean BMI at chatbot onset was 24.00 (SD: 3.82) which remained stable over time (BMI 23.67 (SD: 2.87)). During chatbot monitoring, 45% of patients required artificial supplementation, 11.5% had a gastrostomy tube placed.

Conclusions:: A positive evaluation was obtained both on patient well-being and physicians’ perspective. Also, following these patients with frequent monitoring turned out to help prevent further weight loss due to integrating caloric needs and dietary changes. The solution discussed in this work also provided a significant impact during the COVID-19 emergency.
CHALLENGING DIAGNOSIS OF JUVENILE AMYOTROPHIC LATERAL SCLEROSIS FUS-RELATED DURING COVID-19 PANDEMIC

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Background and Aims:: Juvenile amyotrophic lateral sclerosis (JALS) is a rare motor neuron disease (MND) characterized by progressive degeneration of upper and lower motor neurons. Symptoms of JALS typically begin before age 25, but often in early childhood. We present the case of an apparently sporadic ALS patient carrying a missense mutation in FUS gene where previous infection of SARS-CoV-2 misled clinical investigations.

Methods:: The patient was a 16-year-old boy with mild intellectual disability whose complained progressive hypotonia of the left lower limb.

Results:: At the admission RT-PCR nasopharyngeal swab was positive for SARS-CoV-2 without symptoms. Lumbar puncture was carried out, showing albumin-cytological dissociation and oligoclonal bands. Laboratories revealed high level of inflammatory markers along with monoclonal IgG Kappa component. Neurophysiologic studies showed multi-metamer axonal neurogenic suffering without clear demyelinating alterations. Brain and medulla MRI were normal. Plasma exchange and intravenous immunoglobulins were performed without benefit. Genetic analysis revealed a rare mutation in FUS gene. After five months flaccid tetraparesis with pyramidal signs were evident. He began total dependent of non-invasive ventilation until he died for acute respiratory insufficiency.

Conclusions:: The variability in clinical findings early in the spectrum of MNDs and the lack of any biological diagnostic marker make absolute diagnosis difficult, even more in JALS. The lesson learned in this outbreak of SARS-CoV-2 is that the neurological manifestations attributable to COVID-19 are not so uncommon. In our case laboratory findings were confusing, maybe influenced by the recent SARS-CoV-2 infection, but clinical and neurophysiologic assessment guided us to the correct diagnosis.
NATURAL HISTORY STUDY OF SPINAL MUSCULAR ATROPHY WITH RESPIRATORY DISTRESS TYPE 1 (SMARD1) IN A COHORT OF EUROPEAN PATIENTS

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Background and Aims:: Spinal muscular atrophy with respiratory distress type 1 (SMARD1) is a rare childhood autosomal recessive motor neuron disease, caused by IGHMBP2 gene mutations. The main hallmarks of the disease are diaphragmatic palsy and progressive distal muscular atrophy and paralysis. Currently, there is no treatment and very little data are available on the disease progression. We aim to determine the disease natural course and to define the most suitable functional outcome measures, in the perspective of a future clinical trial.

Methods:: In a cohort of 15 European patients with genetically confirmed SMARD1, we collected clinical data including medical history, neurological, pneumological, cardiological, psychomotor and orthopaedic data. Clinical features and functional motor scales were evaluated every six months.

Results:: We enrolled 15 patients (9 girls) aged between 5 months and 21 years. In 10 cases mothers reported prenatal events, 7 of which resulting in preterm birth. The disease onset was within 5 months for all patients, manifesting with weak crying, feeding difficulties, hypotonia, club foot and acute respiratory distress. All patients need continuous ventilatory support: 13 via tracheostomy while 2 with NIV. G-tube has been performed in 14 out of 15 patients. Head control is reached by 53% of the patients, independent sitting only by 20%. Autonomic dysfunction and scoliosis are observed in all patients.

Conclusions:: SMARD1 is a very rare and severe disease, however it presents heterogeneous clinical manifestations. Our case studies broaden the knowledge relating to the natural course of the disease, providing useful data of the evaluation of possible future therapeutic strategies.
MERCURY MASQUERADING AS MOTOR NEURON DISEASE

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Background and Aims:: The causes of sporadic amyotrophic lateral sclerosis (SALS) remain largely unknown. Heavy metals have long been implicated in MND, and it has been shown that mercury selectively enters human locus ceruleus (LC) and motor neurons. Several case reports of mercury poisoning have demonstrated convincing ALS-like clinical symptoms, leading to postulate a causal relationship

Methods::

He presented with h/o developing abnormal movements of muscle over an upper limb and along with tingling, numbness of both UL and LL with no other neurological complaints. He has fasciculation, over tongue and biceps, with normal power. Reflexes - Biceps, triceps, and knee (3+), rest 2(+). Plantar B/L flexor. He was also having significant proteinuria. His kidney biopsy revealed secondary membranous glomerulonephritis. His EMG revealed – fasciculation noted in Biceps, Brachioradialis, vastus, and gastronemiusà neurogenic EMG S/O ant horn cell disorder, NCS – normal study. Mercury levels were high 24 hr à 57.30 (< 20), His other work-up was negative. On repeated questioning to look for the cause of MND, he came with h/o applying some “BHASM” over for his dermatological condition developed 03 months back prior to these symptoms

Results:: MND is a progressive disorder with median survival three to five years. So correct diagnosis is of utmost importance before committing on motor neuron disease. This case also tells about the importance of proper history taking in neurology to come to proper diagnosis.

Conclusions:: Pt is still on chelating agents and “BHASM” is sent for evaluation of mercury level. His repeat mercury level came down to 30
A SIGHT INTO THE ELDERLY ALS PATIENTS IN EMILIA ROMAGNA REGION: EPIDEMIOLOGICAL AND CLINICAL FEATURES OF LATE ONSET ALS IN A PROSPECTIVE POPULATION-BASED STUDY

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Background and Aims:: Studies on epidemiology ALS epidemiology are numerous and an increasing incidence rate with aging is well known across different Western Countries. Despite this, few studies explored epidemiological and clinical features of the oldest ALS patients.

Methods:: In this prospective, population-based, epidemiological study we investigate demographic, clinical and genotypic features of patients with late-onset ALS in Emilia Romagna Region, where a register has been collecting cases since 2009.

Results:: In the last decade in our region there were 1398 incident cases of ALS (incidence rate:2.83/100,000) of whom 174 (12.45%) were over 80 years old (“oldest” ALS) at diagnosis. Among the oldest, M:F ratio was 0.77, mean age at diagnosis was 83.98(±3.92)years, and 47.13% had a bulbar onset. With increasing age, there was an increment in diagnostic delay, a worse clinical stage at diagnosis, a lower BMI (23.12 vs 24.57,p<0.01), and a higher progression rate (2.14/month vs 1.30,p<0.01), with several comorbidities, and a shorter median survival (25 vs 38 months, p<0.01). Genetic analyses were carried out less frequently in elderly patients and in these group we could not found C9orf72 expansion, according with the fact that being a carrier of this mutation determines a risk of disease onset at a younger age.

Conclusions:: The oldest ALS patients had peculiar clinical features if compared with other adult patients. These genotypic and phenotypic differences between the two groups may underline the presence of different pathogenetic mechanisms and of a different burden of environmental and genetic risk factors triggering the disease onset at different ages.
PROGNOSIS OF PATHOLOGICALLY CONFIRMED JAPANESE AMYOTROPHIC LATERAL SCLEROSIS, A RETROSPECTIVE HOSPITAL-BASED STUDY

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Background and Aims:: We provide medical care for neuromuscular disease patients as a neuromuscular-disease center hospital in Hokuriku area of Japan. It is necessary to understand the prognosis for a better patient’s QOL. We performed retrospective prognostic study to clarify the clinical course and cause of death in pathologically confirmed amyotrophic lateral sclerosis (ALS) patients.

Methods:: We retrospectively reviewed medical records of 120 consecutive autopsied patients between 2008 and 2019. Pathological diagnosis was confirmed when the following two histopathological features were observed. First of them was systematic both upper and lower motor neuronal degeneration, and second was the existence of TDP-43 inclusion body pathology and/or Bunina bodies.

Results:: We identified 54 patients of pathologically diagnosed ALS in this period. Female to male ratio was 16 to 38. Average age of death was 69.6 y.o. (SD=10.6) and median survival time was 45.5 months (SD=50.0). Fifteen patients (28%) chose tracheostomy invasive ventilation (TIV) and 9 patients (17%) decided using non-invasive ventilation (NIV). Female to male ratio of TIV patients was 4 to 11, and that of NIV patients was 1 to 8. TIV prolonged median survival time (105 months), as did NIV (48 months) when compared to non-ventilation supported patients (36 months). Although most common cause of death was respiratory failure due to bronchopneumonia and/or hypoventilation, profiles of complications were depending on the manner of mechanical ventilation.

Conclusions:: From this study, TIV and NIV could improve prognosis of pathologically proved ALS. Respiratory failures due to airway infection were the main cause of death in ALS.
Background and Aims:: Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disorder characterized by upper and lower-motorneurons involvement. However, growing evidence suggests a non-neuronal involvement with a particular attention to autonomic disfunction and consequent cardiovascular complication and sudden-cardiac death. In this contest, many authors focused on arrhythmic complications in ALS patients and in other motorneuron diseases such as Kennedy's Disease (KD). While, Brugada Syndrome (BS) is the most frequent arrhythmia associated with KD, only one case of type2 BS has been described in ALS.

Methods:: To the best of our knowledge, this is the first case report of a patient with lower-limb-onset ALS with type1 BS and previous regular cardiovascular assessment.

Results:: A 58-years-old Caucasian woman was admitted to our neurological clinic for progressive respiratory distress. She was diagnosed with ALS 18 months before. She had no history of cardiovascular disorder and an electrocardiogram (ECG), performed pre-Edaravone therapy, showed a sinusual rhythm in absence of any abnormalities. During hospitalization, pulmonary function tests were performed and a bilevel positive airway pressure ventilation were set-up. At the admission an ECG has been performed and it was suggestive of type3 BS. Therefore a cardiovascular assessment with Flecaïnine induction tests revealed a pattern typical for type1 BS. After that the placement of an implantable cardioverter-defibrillator was suggest.

Conclusions:: ALS is a progressive neuromuscular-disorder with significant mortality. Alongside respiratory failure also cardiovascular complications, especially arrhythmias that may need periodic electrocardiographic surveillance, impact on survival. Therefore, we want to increase evidence that cardiovascular assessment need to be included in ALS management.
INCIDENCE AND PREVALENCE OF AMYOTROPHIC LATERAL SCLEROSIS IN SOUTHWESTERN AND EASTERN FINLAND

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Background and Aims:: Amyotrophic lateral sclerosis (ALS) has been suggested to be relatively common in Finland. We aimed to update the incidence and prevalence data.

Methods:: Patients with ALS diagnostic codes were identified from mandatory administrative registries in the provinces of Southwestern Finland (population c. 430,000) and North Karelia (population c. 170,000). The diagnoses were verified, and data extracted by reviewing the patient records. Incidence period was 2010-2018, and the prevalence date was December 31, 2018.

Results:: We identified 213 patients (54% women) with ALS in Southwest Finland and 102 (54% women) in North Karelia (table 1). Women were older than men at the time of diagnosis in Southwest Finland (p=0.008) with no sex difference in North Karelia (p=0.72). Altogether 55 patients (26%) had been genetically tested in Southwest Finland and 34 (33%) in North Karelia (table 2).

<table>
<thead>
<tr>
<th>Region</th>
<th>New diagnoses 2010-2018 (N)</th>
<th>Age at diagnosis in women (years)</th>
<th>Age at diagnosis in men (years)</th>
<th>Crude incidence, women</th>
<th>Crude incidence, men</th>
<th>Crude prevalence</th>
<th>Age-Standardized prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Southwestern Finland</td>
<td>178 (55% women)</td>
<td>71.6 ± 10.6</td>
<td>67.3 ± 10.6</td>
<td>4.4/100,000</td>
<td>3.9/100,000</td>
<td>11.9/100,000</td>
<td>10.5/100,000</td>
</tr>
<tr>
<td>North Karelia</td>
<td>102 (54% women)</td>
<td>71.0 ± 10.6</td>
<td>67.0 ± 10.6</td>
<td>4.4/100,000</td>
<td>3.9/100,000</td>
<td>11.9/100,000</td>
<td>10.5/100,000</td>
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</tbody>
</table>

Table 1. Incidence and prevalence data by region.

<table>
<thead>
<tr>
<th>Mutations</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>C9orf72</td>
<td>7</td>
</tr>
<tr>
<td>SOD1</td>
<td>11</td>
</tr>
</tbody>
</table>

Table 2. The number of patients with genetic mutations associated with ALS. C9orf72, ; SOD1, .

Conclusions:: ALS is relatively common in both eastern and southwestern Finland. Specific mutation frequency seems to differ by region.
AMYOTROPHIC LATERAL SCLEROSIS: A HOME HEALTHCARE MODEL

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Background and Aims:: Aims of this study is to develop a focused home healthcare model for ALS patients being inspired by the home-care indications in Turner-Stokes model (SIN-SICP Congress 2018).

Methods:: The study lasted approximately two years (a year enrollment started in March 2020 and a subsequent year of follow up). An assigned Case Manager Nurse (CM) supports a network strategy and patient/caregiver training, evaluates clinical patient's conditions every month, collects clinical, social and healthcare data updating ALS-FSR scale every three months.

Results:: Evaluated data include patients with three ALS-FSR evaluations at least and dead ones and exclude patients lost in follow-up phase. Our study includes 24 patients (46% women) and an average age of 66. Most frequent onset is bulbar phenotype (79%). Eating and breath conditions

<table>
<thead>
<tr>
<th>PEG</th>
<th>Tracheostomy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Invasive ventilation</td>
</tr>
<tr>
<td></td>
<td>Non invasive ventilation</td>
</tr>
<tr>
<td></td>
<td>Tracheostomy or PEG refusal</td>
</tr>
</tbody>
</table>

Graphic shows individual ALS-FSR results. Patients with first evaluation ALS < 11
don’t show significant clinical evolutions and nursing care needs; patients with first evaluation ALS > 11 disclose a more variable clinical trend and 63% of them lost more than 3 points in each next evaluation. Home healthcare is divided in Multiprofessionals Home Care (MHC) (75%) and Palliative Home Care (PHC) (25%). During follow up phase, six patients in MHC needed to be assisted in a PHC.

Conclusions:: Patients with first ALS evaluation > 11 disclose a more variable clinical trend: they require a more punctual and frequent oversight both by assigned CM and their Hospital Center.
MODELING AND BIOINFORMATICS IDENTIFY RESPONDERS TO G-CSF IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

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Background and Aims:: Developing an integrative approach to early treatment response classification using survival modeling and bioinformatics with various biomarkers for early assessment of filgrastim treatment effects in amyotrophic lateral sclerosis patients. Filgrastim, a hematopoietic growth factor with excellent safety, routinely applied in oncology and stem cell mobilization, had shown preliminary efficacy in ALS.

Methods:: We conducted individualized long-term filgrastim treatment in 36 ALS patients. The PRO-ACT database, with outcome data from 23 international clinical ALS trials, served as historical control and mathematical reference for survival modeling. Imaging data as well as cytokine and cellular data from stem cell analysis were processed as biomarkers in a non-linear principal component analysis (NLPCA) to identify individual response.

Results:: Cox proportional hazard and matched-pair analyses revealed a significant survival benefit for filgrastim-treated patients. We generated a model for survival estimation based on patients in the PRO-ACT database and then applied the model to filgrastim-treated patients. Model-identified filgrastim responders displayed less functional decline and impressively longer survival than non-responders. Multimodal biomarkers were then analyzed by PCA in the context of model-defined treatment response, allowing identification of subsequent treatment response as early as within 3 months of therapy. Strong treatment response with a median survival of 3.8 years after start of therapy was associated with age, hematopoietic stem cell mobilization, cytokine plasma profiles, and DTI-MRI changes.

Conclusions:: Long-term filgrastim is safe, well-tolerated, and has significant positive effects on disease progression and survival. Model-based biomarker response classification can identify strong individual treatment responders at early stage of therapy and may pave the way to individualized treatment.
BRAIN 18F-FDG-PET SIGNATURE OF ALS WITH SOD1 AND TARDBP MUTATIONS

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Background and Aims:: We evaluated the brain \(^{18}\)F-FDG-PET features of ALS patients with SOD1 (SOD1-ALS) and TARDBP (TARDBP-ALS) mutations, since this field is quite unexplored.

Methods:: Eighteen SOD1-ALS, 14 TARDBP-ALS (carrying the p.A382T mutation), 46 wild-type sporadic patients (sALS), and 40 healthy controls (HC) were enrolled. SOD1-ALS and TARDBP-ALS were compared to sALS and HC, employing the full factorial design and the two-sample t-test of SPM12 (height threshold P<0.001; P<0.05 FWE-corrected at cluster level). Age and sex were included as covariates in all the analyses, spinal/bulbar onset and King’s stage only in comparisons among patients.

Results:: TARDBP-ALS showed a relative hypometabolism in right precentral and postcentral gyrus, superior and middle temporal gyrus and insula, as compared to sALS. TARDBP-ALS showed a relative hypometabolism in bilateral frontal, parietal, temporal and occipital regions as compared to HC. When compared to SOD1-ALS, sALS patients showed a relative hypometabolism in right precentral and medial frontal gyrus, right paracentral lobule, and bilateral postcentral gyrus. As compared to HC, SOD1-ALS showed a relative hypermetabolism in right precentral gyrus and paracentral lobule. sALS patients showed a relative hypometabolism in frontal, temporal and occipital cortices as compared to HC.

Conclusions:: As compared to sALS, TARDBP-ALS patients showed a relative hypometabolism in motor and extramotor regions. The relative hypometabolism in the motor cortex in sALS as compared to SOD1-ALS might be related to the higher prevalence of pyramidal signs in sALS, while the relative hypermetabolism of SOD1-ALS as compared to HC in motor regions might be due to microglial activation.
EXPANDING THE NEUROPSYCHOLOGICAL PHENOTYPE OF ALS: PRELIMINARY FINDINGS

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Background and Aims:: ALS is a neurodegenerative disease primarily affecting the motoneurons. Emerging evidences support the overlap between ALS and frontotemporal dementia (FTD), with cognitive impairment reported in up to 50% of sporadic ALS patients. A recent revision of the ALS diagnostic criteria highlights the importance of assessing the cognitive and behavioral domains, but data collection is still poorly standardized.

Methods:: We enrolled 38 Italian patients with sporadic ALS. Within 3 months from diagnosis, all patients underwent a comprehensive neuropsychological battery of standardized tests for cognitive and behavioral deficits (ECAS), language (SAND), emotion recognition (Ekman test), attention/executive function (Stroop Test) and social cognition (SET) evaluation.

<table>
<thead>
<tr>
<th>Sample demographic and clinical variables</th>
<th>F = 15 (39.5%)</th>
<th>M= 23 (60.5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>age (years)</td>
<td>64.4</td>
<td>12.7</td>
</tr>
<tr>
<td>diagnostic delay (months)</td>
<td>13.5</td>
<td>14.2</td>
</tr>
<tr>
<td>education (years)</td>
<td>10.3</td>
<td>3.9</td>
</tr>
<tr>
<td>ALS-FRSr</td>
<td>40.4</td>
<td>6.1</td>
</tr>
</tbody>
</table>

Results:: Only 9 (24%) patients showed cognitive impairment on ECAS global score. When considering ECAS ALS-specific items, 10 patients (26%) were impaired. SAND partial scores were normal, with the exception of “word repetition” (7 patients, 27%). SET and Stroop test global and partial scores were all within normal limits. 2 patients (5.26%) had defective Ekman 60-faces scores.

Conclusions:: Our results indicate a lower prevalence of cognitive and behavioral impairment in comparison with other studies. Our cohort presents a preservation of emotion recognition, social cognition and attention/executive functions. Language is globally preserved with the exception of non-word phonological errors in some subjects. We aim at expanding the cohort for further cross-sectional and longitudinal evaluation.
SAFETY AND EFFICACY OF FIRST-IN-HUMAN INTRATHECAL TRANSPLANTATION OF HUMAN ASTROCYTES (ASTRORX®) IN ALS PATIENTS: PHASE I/IIA CLINICAL TRIAL RESULTS

Michal Izrael1, Marc Gotkine2, Guy Slutsky1, Yossef Lerner2, Judith Chebath1, Graciela Kuperstein1, Elena Estrin1, Yoseph Caraco3, Tamir Ben-Hur2, Arik Hasson1, Tehila Sonnefeld1, Yafit Stark1, Ariel Revel1, Michel Revel1
1Kaidmatem Ltd., Neurology, Nes-Ziona, Israel, 2Faculty of Medicine, Hebrew university Hadassah Medical center, Neurology, Jerusalem, Israel, 3Hadassah Ein Kerm Hospital, Hadassah Clinical Research Center, Jerusalem, Israel

Background and Aims:: AstroRx® is a cell-based therapy, composed of healthy human astrocytes derived from embryonic-stem-cells. AstroRx® can protect neurons by several mechanisms-of -ction that were demonstrated in in-vitro and in vivo preclinical studies. The hypothesis is that transplantation of AstroRx® can compensate for the malfunctioning of endogenous astrocytes by restoring hampered physiological capabilities, i.e. reducing toxic compounds, reducing oxidative stress and secreting multiple neurotrophic factors.

Methods:: We conducted a Phase I/IIa, Open-Label, dose-escalating Clinical Study to Evaluate the Safety, Tolerability and Therapeutic Effects of Transplantation of AstroRx® in Amyotrophic -lateral- Sclerosis (ALS) patients. Enrolled patients were monitored for 3-months of "run-in period" to record their ALS progression. At the end of the run-in period, 5 patients were injected intrathecally with a single dose of 100*106 AstroRx® and 5 patients with a dose of 250*106 cells. After treatment, the patients were monitored for additional 6-months for safety data and assessment of disease-progression, as compared to the run-in period and for additional 6-months for long safety.

Results:: AstroRx® treatment was well tolerated in both doses and no treatment-related serious-adverse-events nor dose-limiting toxicities related to AstroRx® were reported. A potentially clinically meaningful decline in disease-progression, assessed by the ALS Functional-Rating-Scale-Revised (ALSFRS-R), was observed during the first 3-months of the 6-month follow-up period in both cohorts.

Conclusions:: Single-dose transplantation of AstroRx® is safe and demonstrated a promising efficacy during the first 3-months. These results support a further, randomized-controlled, clinical trial with repeated doses of AstroRx® in ALS patients, in order to prolong the time-span of the clinical effect observed by single-dose.
DYSREGULATION OF LINC-RNAS DURING SKELETAL MUSCLE DEVELOPMENT IN A PATIENT- DERIVED IN VITRO MODEL OF AMYOTROPIC LATERAL SCLEROSIS

Silvia Bonanno¹, Eleonora Giagnorio¹, Claudia Malacarne¹, Patrizia Bossolasco², Erika Salvi³, Donatella Bardelli², Antonia Ratti², Giuseppe Lauria⁴, Renato Mantegazza¹, Stefania Marcuzzo¹
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Background and Aims:: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by progressive degeneration of cortical, bulbar and spinal motor neurons, leading to muscle wasting and paralysis. Although MNs are the crucial targets of the pathogenic process in ALS, there is evidence of an early involvement of skeletal muscles, supporting the concept that it might represent a crucial site of disease pathogenesis. Different causative genes associated to ALS are involved in RNA metabolism. Long-non coding RNA (lncRNAs) are emerging as molecular contributors to ALS pathophysiology because of their role in regulating gene expression. Here we analysed the expression levels of IncRNAs known to be involved in development and maintenance of skeletal muscle in control and ALS patient-derived induced pluripotent stem cells (iPSCs) differentiated towards a myogenic destiny.

Methods:: We differentiated control and ALS patients’ derived iPSCs to myofibres using a small molecule-based protocol. We followed the myogenic process by immunostainings and real-time PCR to assess the expression of skeletal muscle development markers at different time points of the skeletal muscle development.

Results:: We reported a different IncRNAs’ expression pattern in ALS-derived cultures compared to controls, particularly at the mesodermal progenitor, early myocyte and myotube stages of the skeletal muscle differentiation process. Further, we predicted the respective IncRNAs’ mRNA targets identifying specific molecular pathways involved in the development and homeostasis of skeletal muscles, potentially dysregulated over ALS course.

Conclusions:: These data suggest that IncRNAs might be important players in muscle dysregulation in ALS and are candidate for the study of mechanisms contributing to ALS pathogenesis.
DIAGNOSTIC AND PROGNOSTIC ROLE OF PLASMA PHOSPHORYLATED NEUROFILAMENT HEAVY CHAIN (PNF-H) IN AMYOTROPHIC LATERAL SCLEROSIS

Maria Teresa Dell’Abate¹, Chiara Zecca¹, Giuseppe Pasculli², Roberta Barone¹, Rosa Capozzo¹, Maria Rosaria Barulli¹, Serena Arima³, Alessio Pollice⁴, Rosanna Tortelli³, Giancarlo Logroscino¹

¹Center for Neurodegenerative Diseases and the Aging Brain. University of Bari “Aldo Moro” at “Pia Fondazione Card G. Panico” Hospital, Department Of Clinical Research In Neurology, Tricase, Italy, ²La Sapienza University, Department Of Computer, Control, And Management Engineering Antonio Ruberti (diag), Rome, Italy, ³University of Salento, Department Of History, Society And Human Studies, Lecce, Italy, ⁴University of Bari “Aldo Moro”, Department Of Economics And Finance, Bari, Italy

Background and Aims:: The phosphorylated neurofilament heavy chain (pNf-H) is a promising putative biomarker in Amyotrophic Lateral Sclerosis (ALS). We examined pNf-H concentrations in plasma of ALS patients to investigate its potential as a diagnostic and prognostic biomarker.

Methods:: Incident ALS cases enrolled in a population-based registry were retrospectively selected and matched by sex and age with a cohort of healthy volunteers. Plasma pNf-H levels were measured by an ELISA kit (Neurofilament pNf-H-high sensitive ELISA, Euroimmun) and correlated with clinical parameters. Discrimination ability of pNf-H was tested using Receiving Operating Characteristic (ROC) curves. Kaplan-Meier (KM) univariate analysis was carried-out to determine the survival probability based on plasma pNf-H; univariate and multivariable Cox proportional hazard models were performed to estimate the effect of plasma pNf-H on survival, adjusted for clinically relevant covariates.

Results:: Plasma pNf-H was significantly higher in patients compared to controls. An optimal cut-off of 39.74 pg/ml discriminated cases from controls with 75% sensitivity and specificity. Bulbar-onset cases had higher levels of plasma pNf-H compared to spinal onset (p=0.0033). Furthermore, plasma pNf-H positively correlated with disease progression rate (r=0.19, p=0.031). Survival probability was no different among cases stratified according to pNf-H median value (101pg/mL) (log-rank test χ²= 0.5; p=0.49). In Cox PH regression models plasma pNf-H was not independently associated with a reduced survival in cases (aHR 1, 95% CI 1-1, p = 0.028).

Conclusions:: Our findings confirmed the potential utility of plasma pNfH as a diagnostic biomarker in ALS. However, further evaluations in longitudinal data are needed to corroborate its prognostic value.
Background and Aims:: Neurodegenerative disorders are associated with high burden for patients, their families and the society, with overload of the professionals. We addressed the professional and personal insights and expectations of the latter, including during the COVID-19 pandemic.

Methods:: A survey was developed and made available in google forms (https://docs.google.com/forms/d/1-Gv5gtrl8qb1r7C7ChpJnxs-a4ynIS6sGMu-70wm3Ss/edit#responses), between 26/10-15/11/2020, to professionals working in the neurodegenerative field. Three sections were considered, addressing: characterization of the respondents; patient-professional relation; pathophysiology, genotype-phenotype, pharmacological perspectives. Means and frequencies were calculated. Differences between those working >15 vs =<15 years were assessed using Fisher exact test. P<0.05 was significant.

Results:: Eighty-two professionals, from 5 continents, most Europeans, answered. Most were fullfilled with work, 47 worked >15 years, 67% for >=4 days/week. Clinicians described positive impact on patients/families. Almost all had strategies to cope with the diseases' devastating nature, not affected by the COVID-19 in 44.3% or sometimes in 35.7%. Causative genetic interplay, protein aggregations and common neurodegenerative pathways, with ageing impact, justified a partial or continuous spectrum, with high levels of congruence between respondents =<15 vs >15 years/ work. Most believed in disease improvement, available within 5 years, but a cure only in the far future.

Conclusions:: Professionals working in the neurodegenerative field are satisfied and motivated. Coping strategies may, nevertheless, be influenced by the COVID-19. Causative genetic interplay, protein aggregations, common neurodegenerative pathways and ageing play relevant roles, and justify partial/continuous spectrum, with high levels of congruence between professionals. A cure is not expected in the near future, but hope exists.
CLINICAL AND GENETIC SPECTRUM OF AMYOTROPHIC LATERAL SCLEROSIS IN A TUNISIAN SERIES

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Background and Aims:: Few studies looking at Amyotrophic Lateral Sclerosis (ALS) among African populations were published. Our aim was to describe clinical characteristics of Tunisian ALS patients and to explore the main candidate genes and their potential associations with ALS phenotype.

Methods:: We included ALS patients followed up in the department of Neurology of Razi University Hospital over a 17-year period. For genotyping, analysis of SOD1, FUS, and TARDBP were sequenced by Sanger, while C9orf72 expansion was performed using PR-PCR. Genetic study was conducted at IRCCS Istituto Auxologico Italiano in Milan and the sequencing platform of faculty of Medicine of Tunis.

Results:: We included 201 patients. In this cohort we had 24 familial ALS and 12 Juvenile ALS form (JALS). Median age of ALS onset was 54.93 years and sex-ratio was 2.0. Among classic forms 76.3% had spinal onset whereas bulbar was seen in 20.1% of patients. Consanguinity was present in 66.7% of JALS. The median survival among JALS was 15 years. TARDBP mutation p.G294A was responsible for 12.93% of cases. SOD1 mutations were present in 10.45% of patients. C9ORF72 repeat expansion was found in 4.47% and no pathogenic variant of FUS were observed. For JALS, we identified 2 Alsin Gene mutations and one SOD1 gene mutation.

Conclusions:: We found a higher frequency of Juvenile forms, an overall slower ALS progression and a high frequencies of mutations in TARDBP, SOD1 and C9ORF72 genes. These findings in a large North African cohort help to shed lights on phenotype and genotype peculiarities in this population.
ALS AND COGNITION IMPAIRMENT

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Background and Aims:: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder involving primarily motor neurons in the cerebral cortex, brainstem and spinal cord. Despite the increased awareness of ALS as a multi-system disorder, the cognitive status of most ALS patients attending clinics remains unknown.

Methods:: The study aimed to evaluate cognitive profile and behavioral impairment in ALS patients who came for the first time in Neurology dept., UHC Mother Teresa, Tirana. Methods: In total, 28 patients with the diagnosis of ALS according to the revised El Escorial criteria and 46 age-, education- and gender matched controls participated in the study. Each case was screened for cognitive dysfunction (MOCA; ECAS) and behavioral impairment (ADL; IADL, Quality of life and FBI).

Results:: The mean age of the participants at time of assessment was 59.4 ± 10.1 years and 67.9% were men. ALS patients had a significantly higher frequency of impairment in MOCA, language, verbal fluency, executive function, memory and total ECAS (p value<0.05). Executive function is the most affected domain, followed by memory and language.MOCA and total ECAS was more affected in patients with bulbar onset disease compared to spinal onset( p value respectively 0.065 and 0.099). Respiratory dysfunction was associated with significantly lower scores on MOCA and executive function (0.091 and 0.104 respectively). Most of patients had minimal behavioral impairment.

Conclusions:: These findings suggest that ALS does not selectively affect only the pyramidal motor system, but rather is a multisystem neurodegenerative disease.
Background and Aims:: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder of motor neurons. Spread of pathology to other brain areas leads to development of non-motor symptoms (NMSs). These usually remain undiagnosed because of overwhelming motor problem and are responsible for significant distress to the patient. Our objective was to explore the burden of various NMSs of patients with ALS, compare between limb-onset and bulbar-onset patients, and to correlate with severity and duration of disease.

Methods:: Fifty patients with ALS diagnosed according to revised El Escorial Criteria and 50 healthy controls were included in this study. They were assessed with NMS Questionnaire, Beck's Depression Inventory, Center for Neurologic Study-Lability Scale, Drooling Frequency and Severity Scale, Epworth Sleepiness scale, Bengali Mental State Examination, and Frontal Assessment Battery and relevant statistical analyses were carried out.

Results:: The patients with ALS had significantly increased prevalence of almost all NMSs compared to controls. There was also significant increase in depression, suicidal ideation, pseudobulbar affect, and daytime sleepiness in patients with ALS. The bulbar onset subgroup had significantly increased daytime drooling, dysphagia, nausea and vomiting, whereas the limb onset subgroup reported increased frequency of leg swelling. Executive dysfunction was detected in 24% of patients with ALS and 9.8% had mild cognitive impairment. Weight loss, frequency of falling, insomnia, unpleasant nocturnal leg sensations, difficulty having sex, depression, and cognitive impairment increased significantly with an increase in severity of the disease.

Conclusions:: NMSs were significantly more prevalent in patients with ALS. Some NMSs worsened with advancement of the disease.
TWO CASES OF UNILATERAL WASTING AND WEAKNESS OF DISTAL UPPER LIMB: SIMILAR ONSET AND DIFFERENT DIAGNOSIS IN YOUNG PATIENTS

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Background and Aims:: We presented two patients with unilateral weakness and wasting of distal upper limb at onset.

Methods:: A 20-years-old woman (patient 1) and a 16-years-old man (patient 2) developed weakness and wasting of left distal upper limb, subsequently spreading to forearms. Clinical, laboratory, neurophysiological and MRI assessment were performed.

Results:: Both patients exhibited weakness and hypotrophy of forearms and hands muscles on neurological examination, unremarkable laboratory and cerebrospinal fluid work-up, including anti-gangliosides antibodies, and brain MRI. Patient 1: upper and lower limb motor evoked potentials (MEPs) were absent bilaterally. Somatosensory evoked potentials (SSEPs) and nerve conduction study (NCS) were normal. Electromiography showed chronic denervation signs in upper limbs muscles. Cervical spine MRI was normal. Patient 2: SSEPs detected prolonged latencies in lower limbs; upper and lower limb MEPs were absent bilaterally. Electromiography showed chronic denervation signs in upper limbs muscles, with spared brachioradialis muscles. NCS revealed left ulnar axonal neuropathy. Cervical spine MRI, performed on neutral and flexion positioning, detected straight cervical spine, posterior loss of attachment and anterior displacement of extradural space with anterior cord flattening, C4-C7 epidural contrast enhancement on T1-sequence. He was unsuccessfully treated with intravenously immunoglobulins. At one-year follow-up, patient 1 developed diffuse upper and lower motor neuron signs, consistent with motor neuron disease (MND), whereas patient 2 was stable, consistent with Hirayama disease (HD).

Conclusions:: In early stages, HD and MND may be difficult to differentiate, leading to misdiagnosis and mistreatment. Our findings highlight rarity of HD and key role of clinical, neurophysiological and MRI investigations in differential diagnosis.
POTENTIAL OF IMMUNOGLOBULINE TREATMENT IN MOTOR NEURON DISEASES ASSOCIATED TO BLOOD- BRAIN BARRIER DAMAGE

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Background and Aims:: Motor neuron diseases (MND) are inherently complex and may result in several different diagnoses with challenging treatment. Here, we report two cases of MND showing clinical improvement after immunoglobuline infusion.

Methods:: The first case is a 39-year-old man with a history of proximal upper limbs hyposthenia and fluctuating slurred speech that had appeared one year prior after a flu syndrome. In time, symptoms grew to proximal upper limbs amyotrophia and tongue atrophy with fluctuating dysphagia. The electromyogram showed a chronic neurogenic pattern on the affected muscles with localized acute denervation. The second case is a 59 years old man that showed an acute onset of diffuse muscle weakness and fasciculations, with associated respiratory insufficiency and a recent history of severe weight loss. He presented neurogenic patterns with acute denervation and fasciculation potentials in all the muscles examined at the electromyogram.

Results:: In the first case, due to the persistence of high levels of CRP, the patient underwent a CSF exam that showed blood-brain barrier damage with systemic oligoclonal bands. An intravenous immunoglobulin therapy showed a prompt improvement both in hyposthenia and in bulbar symptoms. Also in the second case, the CSF exam showed blood barrier damage, and intravenous immunoglobulin therapy showed a remarkable improvement both in muscular strength and in respiratory function.

Conclusions:: These cases confirm that immunoglobulins have therapeutic value in treating MND in presence of blood-brain barrier damage, suggesting their careful consideration to treat selected cases.
SYMPTOMATIC C9ORF72 MUTATION IN NON-FLUENT APHASIA WITHOUT NEUROIMAGING SIGNS OF CEREBRAL ATROPHY: A CASE STUDY

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Background and Aims:: Expansion mutations in the C9orf72 gene may cause familial amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Diffuse subcortical brain atrophy, while absent in asymptomatic patients, is frequent in symptomatic C9orf72 subjects, suggesting a direct association with active disease. Therefore, neuroimaging studies may be used as follow-up biomarker in patients carrying the mutation. Here, we describe a case of initial non-fluent aphasia in a C9orf72 patient

Methods:: A 61 years old female patient came to our attention for a rapid onset of dysarthria with agrammatic speech and depressed mood that appeared 18 months prior, following an important grieving. Due to the patient’s familiarity for neurodegenerative disorders in her maternal lineage (sister and grandmother affected by ALS, mother affected by Alzheimer’s disease

Results:: Electromyograms, cerebral FDG PET and a high camp cerebral MRI, all resulted normal. Neurological examination was normal, except for agrammatic speech and saccadization of pursuit at ocular movements’ examination. The NGS analysis revealed a C9orf 72 expansion (137 repetitions of G4C2). Following further evaluations after a year of clinical stability, the patient showed progressive pyramidal and frontal release signs.

Conclusions:: Our patient did not show alterations in brain imaging in spite of having a symptomatic C9orf72 mutation and a long history of language disturbances. This report remarks the complexity of the neurodegenerative process and its molecular-clinical relationships along the C9orf72 related ALS/FTD spectrum.
COMPREHENSIVE APPROACH: NEUROGENESIS, EXTRACELLULAR MATRIX, AUTOPHAGY AND IMMUNE DYSFUNCTION AS TREATMENT TARGETS IN NEURODEGENERATION AS IN ALS - REORGANIZING PHYSIOLOGICAL REPAIR

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Background and Aims:: Constant physiological remodeling and repair are increasingly dysfunctional in several essential brain systems during neurodegenerative disorders. Once chronic neuroinflammatory mechanisms are activated, a machinery of major cytokines - among them an upregulated TGF-β system - are pushing this process forward. By hitting the TGF-β system as such crucial single target, our aim was to reach many critical downstream mechanisms of neurodegeneration at one time for a long-term treatment approach.

Methods:: A new LNA (Locked Nucelotide Acid) - 16mer gapmer antisense molecule targeting exclusively the human Transforming Growth Factor β Receptor Type II (TGBR2) was designed and validated in vitro. A regulatory 13-week GLP program with repeat intrathecal applications in physiological saline (controls and 3 dose ranges) was performed in cynomolgus monkeys.

Results:: With excellent tolerance and a no observed adverse effect level (NOAEL), drug effects could be attributed to specific downregulation of the target molecule and local / systemic dose dependent tissue levels. Functional activities at the level of mRNA - modulation in stem cell regulation, autophagy, extracellular matrix and immune activation also led to a dose dependent increase in neurogenesis in hippocampus, subventricular zone, and spinal cord of these healthy monkeys. As mode of action, canonical - more so non-canonical - signaling of TGF-β pathways could be identified.

Conclusions:: Single-drug pharmacological intervention has the potential to safely and efficiently address some of the most relevant pathophysiological mechanisms in neurodegenerative disorders at once and now needs clinical development. Brain and spinal cord regeneration in neurodegenerative disorders may have a realistic future perspective.
A SYSTEMATIC REVIEW ON RISKS OF NEURODEGENERATIVE DISEASES IN PROFESSIONAL SPORTS.

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Background and Aims:: Previously published literature reported an association between sports and neurodegenerative diseases (ND), in particular, motor neuron disease (MND), amyotrophic lateral sclerosis (ALS), dementia, mild cognitive impairment (MCI), Chronic Traumatic Encephalopathy (CTE), and Parkinson’s disease (PD). The aim of this systematic review (SR) was to gather available evidence on professional sport as a potential risk factor for NDs.

Methods:: This SR was performed following the methodology stated in the Cochrane handbook and the PRISMA statement. Available literature was searched on PubMed, Discovery, and the Cochrane databases. All case-control and cohort studies reported professional sport as a risk factor for the considered NDs were included.

Results:: Searches yielded 7390 records, and 19 articles were included. Results showed an overall 3.53 (95%CI 2.72-4.57, p<0.001) HR of death due to NDs in professional players and, in particular, a HR of 3.87 for dementia (95%CI 2.86-5.24, p<0.001), 4.33 for MND (95%CI 2.05-9.15, p<0.001) and 2.15 for PD (95%CI 1.17-3.96, p=0.01). Another cohort study found a 3-times higher mortality rate due to NDs in football players (SMR 2.83, 95%CI 1.36-5.2), and an almost 4-times higher mortality rate for ALS (SMR 4.31, 95%CI 1.73-8.87) and for AD (SMR 3.86, 95%CI 1.55-7.95). One study reported a 5-times higher prevalence of MCI in retired football players, who reported ≥3 concussions, and another study reported an association between CTE and boxing (OR 9.50, 95%CI 1.73-52.12, p=0.01).

Conclusions:: Preliminary data showed significant association between NDs and the exposure to some sports at a professional level, such as boxing, soccer and football.
ATYPICAL ONSET OF AMYOTROPHIC LATERAL SCLEROSIS: EIGHT CASES REPORT

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Background and Aims:: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that affects both lower motor neurons (LMN) and upper motor neurons (UMN). There is a marked phenotypic heterogeneity between cases. The aim of our study is to present the atypical onset of this disease.

Methods:: This is a retrospective and descriptive study of eight clinical cases of defined ALS with atypical onset, diagnosed in our department.

Results:: Four men and four women aged 30 to 66 years. Unusual onset were: 1) A woman with inaugural neuromyotonia, revealed by painful tonic contractures, cramps, fasciculations, electroneuromyography (ENMG) showed neuromuscular hyperexcitability, etiological assessment remained negative. 2) and 3) Two men with inaugural acute respiratory failure. 4) A young woman presented subacute pseudo-myositis, the initial ENMG showed a myogenic appearance, follow up ENMG disclosed diffuse denervation patterns. 5) A man with isolated pseudobulbar palsy syndrome lasted for more than 4 years before the onset of signs of LMN impairment. 6) A woman with a Flail Leg, associated with sicca syndrome whose treatment was not effective, rapidly progressing to diaphragmatic involvement that required noninvasive ventilation. 7) A woman initially diagnosed with probable Chronic inflammatory demyelinating polyneuropathy with moderate sensory deficit in the lower limbs, without any improvement under IVIg treatment. She died 2 years later. 8) A man with chronic right brachial monoparesis, which remained isolated with focal involvement of LMN in C6-T1 levels for 6 years.

Conclusions:: An unusual onset of ALS necessarily leads to differential diagnoses, clinical and ENMG monitoring remains the key to diagnosis.
PHASE 3 TRIAL OF ULTRA-HIGH DOSE METHYLCOBALAMIN IN EARLY-STAGE AMYOTROPHIC LATERAL SCLEROSIS

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Background and Aims:: In the post-hoc analyses of our previous study conducted to verify efficacy and safety of ultra-high dose methylcobalamin against patients diagnosed by the revised El Escorial criteria (rEEC), methylcobalamin may prolong survival and retard symptomatic progression without major side effects if started early (≤12 months' duration). The objective of next trial: The Japanese Early Stage Trial of High Dose Methylcobalamin for Amyotrophic Lateral Sclerosis (JETALS) is to reconfirm the efficacy and safety of ultra-high dose methylcobalamin for ALS patients in their early stages.

Methods:: JETALS is a prospective, multicenter, placebo-controlled, double-blind, randomized phase III study conducted at 25 tertiary neurology centers in Japan. Patients diagnosed with ALS corresponding to the categories of definite, probable, or probable-laboratory supported in the updated Awaji criteria (UAC) within 12 months from onset were registered at observation period, then patients whose the Revised ALS Functional Rating scale (ALSFRS-R) total score has decreased by 1–2 points during 12 weeks proceeded to the treatment period and were randomized at a 1:1 ratio to receive intramuscular injection with methylcobalamin 50 mg or placebo twice a week for 16 weeks. We adopted UAC for the first time in the world to our knowledge, which revealed a higher sensitivity compared to rEEC. The target number of subjects is 128. The primary endpoint is changes in the ALSFRS-R total score at 16 weeks.

Results:: This study was started in October 2017 and 130 patients have been enrolled by the end of October 2019.

Conclusions:: The results of JETALS will be presented at the congress.
BRAIN ENERGY METABOLISM IN ALS: A PHOSPHORUS-31 MAGNETIC RESONANCE SPECTROSCOPY STUDY

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Background and Aims:: In vitro and animal studies indicate that bioenergetic dysfunction in brain is an important pathophysiological mechanism in amyotrophic lateral sclerosis (ALS). We aimed to characterise for the first time brain energy metabolism in ALS patients using phosphorus-31 magnetic resonance spectroscopy (³¹P-MRS).

Methods:: Brain spectroscopy was acquired from motor regions in twenty patients and ten age and gender-matched healthy controls. Spectroscopic parameters were estimated with AMARES algorithm and expressed as a proportion of total phosphorus signal. Revised ALS Functional Rating Scale (ALSFRS-R), slow vital capacity (SVC), and upper motor neuron score (UMNS) were assessed.

Results:: Phosphocreatine was reduced in the pons in patients compared to controls (p=0.002) and retained significance after adjusting for voxel partial brain fraction and age. Lower phosphocreatine was associated with greater disability on ALSFRS-R and lower SVC. No differences were found in motor cortex or deep white matter.

Conclusions:: Decreased phosphocreatine is a hallmark of bioenergetic dysfunction in mitochondrial cytopathies. Correlations with ALSFRS-R and SVC suggest clinical relevance. This study is the first to illustrate the presence of cranial bioenergetic dysfunction in vivo in ALS patients, and illustrates the potential of ³¹P-MRS as a biomarker of mitochondrial dysfunction. Acknowledgements: We thank the study participants and Prof Iain Wilkinson for establishing the technique. This work was supported by: the NIHR Sheffield Biomedical Research Centre for Translational Neuroscience, British Medical Association Vera Down, and Neurocare/Ryder Briggs Trust. This work was published in (1). References: (1) Sassani, M., et. Al (2020). "Magnetic resonance spectroscopy reveals mitochondrial dysfunction in amyotrophic lateral sclerosis." Brain 143(12): 3603-3618.
TWO CONTRASTING CLINICAL MANIFESTATIONS OF AMYOTROPHIC LATERAL SCLEROSIS (ALS) RELATED TO FUS MUTATIONS

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Background and Aims:: Alterations of the Fused in Sarcoma FUS gene have been put in relation with an array of neurodegenerative disorders, including juvenile ALS with an aggressive progression. Here, we describe two patients carrying FUS mutations and showing contrasting ALS phenotypes and different histories of disease progression

Methods:: The first patient is a 43-year-old male with a clear family track record for ALS (mother, maternal uncle and maternal grandfather) who initially developed a neurogenic monomelic amyotrophy that remained restricted to the right lower limb for more than one year. He later showed a quick and diffuse involvement of all limbs, bulbar and respiratory muscles. The second patient is 50-year-old male with no history of neurological diseases except for a sister who died of a cerebral malignancy at the age of 40. The patient developed in 2007 a typical form of ALS that a few years later required the positioning of tracheostomy and percutaneous gastrectomy. The patient is still alive

Results:: A NGS analysis reported a heterozygous mutation of Arg>521Cys in the first patient’s FUS gene. The second patient was found to carry a heterozygous variant in c.667_672delCGGCGG, p. GLY223_Gly224 in exon 6 of FUS gene.

Conclusions:: Although in the first patient the FUS alteration results in phenotypes in line with other cases previously described in literature, the disease’ hallmarks in the second patient are not commonly reported in FUS-related ALS. These two cases confirm the wide clinical spectrum that may be related to FUS mutation, prompting to further studies to shed light on its complex pathogenetic mechanisms.
Background and Aims:: ALS (amyotrophic lateral sclerosis) is a multifactorial disorder. Some pathogenic genetic variants are responsible of many cases.

Methods:: To expose a case report about a ALS patient with two probably pathogenic new variants in TBK1 and ANG genes.

Results:: A 63-years-old woman experienced clumsiness in her right leg in the last year. In the last month, she also complained of clumsiness in her right hand. She had not any relevant personal or family medical history except to a sibling with spasticity. In the neurological examination, we detected right hemiparesis, hyperreflexia with clonus, right Babinski sign, and spastic gait. In electromyography, we found denervation activity. Neuroimaging studies were normal. With these findings, the ALS diagnosis was made. We also requested analysis of genes associated with ALS. The result was the presence of two probably pathogenic variants in the TBK1 c.1318C>Tp.(Arg440*) and ANG c.394G>Tp.(Glu132*) genes. We sequenced these in his brother, who was also carrier of both.

Conclusions:: The (TBK1):c.1318C>Tp.(Arg440*) variant has not been reported before, and it is not present in population databases. This variant is expected to lead in an absent or altered protein product. A similar variant (R357X) was reported in a ALS patient. The (ANG):c.394G>Tp.(Glu132*) variant has not been reported before, and it is not present in population databases, either. It causes a premature stop signal at codon 132 of the ANG gene. The alteration is expected to lead in an absent or altered protein product.
MONOMELIC AMYOTROPHY OF UPPER LIMB. 4 CASE REPORTS

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Background and Aims:: Monomelic amyotrophy represent a clinical-electrical and radiological syndrome similar to Hirayama disease, but involving multiple etiologies

Methods:: Nous rapportons les observations cliniques de 4 patients présentant une amyotrophie et une faiblesse progressive d'un membre supérieur, proximale dans 3 cas et distale dans un seul cas, unilatérale dans 3 cas et bilatérale dans un seul cas.

Results:: L'électromyogramme a montré des lésions neurogènes cervicales localisées, et l'imagerie par résonance magnétique (IRM) a montré un hypersignal dans les cornes antérieures du cordon cervical correspondant aux myotomes affectés. L'évaluation étiologique a montré une éosinophilie chez un patient. Deux patients pratiquaient un sport intensif (musculation, art martial), un patient avait des antécédents de traumatisme cervical et un patient avait une infection dans les jours précédant la présentation clinique. Les patients ont reçu un traitement symptomatique avec rééducation fonctionnelle et l'évolution a été marquée par une stabilisation des symptômes.

Conclusions:: Monomelic atrophies correspond to ischemic lesions of the anterior horns, sometimes visible on MRI in the form of hypersignal. The location and extent of ischemic spinal cord involvement vary from different cases. Confusion with Hirayama disease is possible when ischemia is confined to the anterior territories of the C7-D1 levels. Chronic spinal cord ischemia may result not from direct compression of the anterior spinal artery, but also from increased intramedullary pressure, leading to local microcirculation disorder. However, other aetiologies are increasingly implicated in the pathogenesis of the disease, such as infection by viruses which have tropism for the anterior horn and certain immunoallergic disorders.
ALSFRS SCORES IMPROVED AFTER MULTIPLE INFUSIONS OF AUTOLOGOUS ADIPOSE TISSUE-DERIVED STEM CELLS IN ALS PATIENTS

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Background and Aims:: The aim of the study was to confirm the safety and to investigate the efficacy of intravenous administration of autologous adipose-derived stem cells (ADSCs) for amyotrophic lateral sclerosis (ALS).

Methods:: Six ALS patients were treated with 4.3-8.7x10⁷ ADSCs administered intravenously three times at 1-2 month intervals. Patients who had already been diagnosed with ALS at other hospitals and who were willing to participate in the study and who could come to the study hospital for intravenous infusion treatment were included in the study. The patient was examined by multiple physicians, including neurologists, and followed up with interviews of the patient and caregivers for up to 3 months after administration.

Results:: One patient died of ALS progression. The patient's ALS Functional Rating Scale (ALSFRS) was 35 before dosing and 14 after dosing. The ALSFRSs of the other 5 patients were 35 to 45, 35 to 27, 46 to 46, 38 to 23, and 16 to 11 before and at 3 months after 3 doses, respectively. No adverse events were observed.

Conclusions:: ADSCs can be collected with minimal invasion, cultured in a serum-free medium, and administered intravenously repeatedly in a safe manner. No side effects were observed. Since this study was open-label and there was no control group, judgments of efficacy must be made with caution. However, the fact that ALSFRS was maintained or improved in 2 of the 6 patients suggests that this treatment may be effective. The results of this study provide a rationale for future trials to verify the efficacy of this treatment.
EFFICACY AND SAFETY OF ULTRA-HIGH DOSE METHYLCOBALAMIN IN EARLY STAGE AMYOTROPHIC LATERAL SCLEROSIS: RESULTS OF A RANDOMIZED, DOUBLE-BLEND, PHASE 3 TRIAL (JETALS)

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Background and Aims:: Clinical and non-clinical studies have shown that intramuscular ultra-high dose methylcobalamin is potentially effective against amyotrophic lateral sclerosis (ALS). Post hoc analyses in a previous phase 2/3 clinical trial showed that methylcobalamin prolonged survival time and arrested functional decline compared to placebo in patients registered within 12 months of ALS onset. The objective of the next trial: The Japanese Early Stage Trial of High Dose Methylcobalamin for Amyotrophic Lateral Sclerosis (JETALS), was to reconfirm the efficacy and safety of ultra-high dose methylcobalamin for ALS patients in their early stages. (NCT03548311)

Methods:: JETALS was a prospective, multicenter, placebo-controlled, double-blind, randomized phase 3 study conducted at 25 tertiary neurology centers in Japan. Eligible patients, diagnosed within 12 months of onset according to the updated Awaji criteria, were randomized at a 1:1 ratio to receive intramuscular injections of 50 mg of methylcobalamin or placebo twice weekly for 16 weeks. The target number of subjects was 128. The primary endpoint was changes in the ALSFRS-R total score from baseline to week 16 weeks.

Results:: A total of 130 patients were randomly assigned to methylcobalamin or placebo group, and 126 patients completed the trial. The changes in the ALSFRS-R total score from baseline to 16 weeks were significantly lower in methylcobalamin group. The incidence of adverse events was similar between the 2 groups.

Conclusions:: Ultra-high dose methylcobalamin was found to be efficacious in slowing functional decline compared with placebo and to have a high safety profile in patients with early-stage ALS.
A PHASE I DOSE ESCALATION STUDY OF BOSUTINIB FOR AMYOTROPHIC LATERAL SCLEROSIS: INDUCED PLURIPOTENT STEM CELL-BASED DRUG REPURPOSING FOR AMYOTROPHIC LATERAL SCLEROSIS MEDICINE (IDREAM) STUDY

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Background and Aims:: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease caused by the loss of motor neurons, and the development of an effective medicine is urgently required. Induced pluripotent stem cell-based drug repurposing identified a Src/c-Abl inhibitor, bosutinib which is approved for the treatment of chronic myelogenous leukemia (CML), as a candidate for molecular targeted therapy of ALS.

Methods:: A Phase 1, open-label, multi-center, 3+3 dose escalation study was conducted to evaluate the safety and tolerability of bosutinib in ALS patients. The preliminary efficacy of bosutinib was also evaluated using ALS clinical score ALSFRS-R, and predictive biomarkers were explored. Patients received escalating doses of bosutinib starting from 100 mg QD (quaque die) up to 400 mg QD based on dose limiting toxicity (DLT) occurrence.

Results:: A total of 20 participants were enrolled, 13 of whom received bosutinib treatment and 12 were included in the safety and efficacy analyses. No DLTs were observed up to 300 mg QD whereas three DLTs were observed at 400 mg QD cohort. Safety profile was consistent to what is known for CML treatment, and neither new safety signal nor ALS-specific adverse events were observed. Although the study was conducted in a small number of cases, bosutinib administration was found to halt progression in some of the participants, and 5 of 9 patients showed stable disease. Furthermore, a biomarker enriched highly effective patients.

Conclusions:: Bosutinib administration up to 300 mg QD was safe and well tolerated with promising efficacy for motor symptoms in ALS. (NCT04744532)
MICRONNA-129: AN EMERGING THERAPEUTIC TARGET FOR AMYOTROPHIC LATERAL SCLEROSIS

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Background and Aims:: MicroRNAs are increasingly involved in the pathophysiology of Amyotrophic Lateral Disease (ALS). Therapeutic approaches have not been able to modify its course and outcome, so ALS is a source of interest for modern research.

Methods:: We systematically searched and critically appraised studies in PubMed which explored the role of miRNA-129 in the pathophysiology of ALS along with studies relevant to the use of antisense oligonucleotide (ASO), anti-mRNAs and adeno-associated virus.

Results:: The deregulation of miR-129 in ALS is manifested by the upregulation of miR-129-5p, which has a major influence on neurons, and by the overexpression of pre-miR-129-1 with a major effect on the axons. This upregulation has been shown to cause downregulation of the RNA-binding HuD protein, which is encoded by the ELAVL4 gene. Administration of the miR-129-5p ASO inhibitor to a rodent with SOD1 ALS, resulted in a significant increase in survival and an improvement in the neuromuscular phenotype. In axons, overexpression of pre-miR-129-1 inhibits their growth and differentiation by silencing the HuD gene in vitro, while inhibition of pre-miR-129-1 using anti-mRNAs extended survival, maintained body weight and prevented loss of strength. Delivery of ASO or anti-mRNAs in patients with SOD1 ALS can be achieved with a single intrathecal injection of an adeno-associated virus.

Conclusions:: MiR-129 emerges as a therapeutic target that can be modified either by inhibition through the ASO of miR-129-5p or by inhibition of the action of pre-miR-129-1 with anti-mRNAs and adeno-associated virus can contribute in order for these inhibitors to be delivered in patients with SOD1 ALS.
INCIDENCE PATTERN UPDATE OF AMYOTROPHIC LATERAL SCLEROSIS IN THE PROVINCE OF FERRARA

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Background and Aims:: Amyotrophic Lateral Sclerosis (ALS) is a rare progressive neurodegenerative disease affecting motor neurons with an average annual incidence of 1-3 cases/100,000 people worldwide. Its etiopathogenesis is unknown and several possible genetic and environmental factors have been proposed. This study updates the epidemiological data on ALS in the province of Ferrara, northern Italy, between 2017 and 2020, integrating the results with previous studies.

Methods:: The average population was 345,538 inhabitants (51.9% females). 38 patients were included (20 men and 18 women), according to the revised El Escorial diagnostic criteria. We reviewed all the possible sources of case collection.

Results::

Mean crude incidence rate was 2.75/100,000 inhabitants/year (95% CI 1.95-3.76), 3.01 males and 2.51 females; standardized incidence rate to the Italian population of 2.37/100,000 inhabitants/year, 2.08/100,000 inhabitants/year to the European population. Mean age of diagnosis 70 years (SD ± 7.96). Peak incidence: between 60 and 69 years, with a rate of 9.36/100,000 inhabitants (CI 95% 5.55-14.79) in general population (11 in males and 7.83 in females). Rate in urban centers: 2.86/100,000 population/year, in rural centers 2.53/100,000 population/year. Male to female ratio: 1.11. 57.89% had spinal onset, 21.05% bulbar onset and 15.79% mixed onset.

Conclusions:: There is a persistent increase in new diagnoses compared with studies of the early 2000s in accordance with literature, suggesting the importance of environmental factors in genetically
predisposed people. Improvement in diagnostic criteria, increase in average life span (with a greater risk of neurodegenerative diseases), greater prevalence in males and greater frequency of spinal onset mode are evident.
EVALUATION OF SPINAL AND CORTICAL MAGNETIC STIMULATION TOGETHER WITH MSCAN MUNE IN THE EARLY STAGES OF THE DISEASE IN THE DIAGNOSIS OF ALS.

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Akdeniz University Faculty of Medicine, Neurology Department, Antalya, Turkey

Background and Aims:: Electrophysiological methods are still the leading investigations in the diagnosis of ALS. Although needle EMG is the main finding in demonstrating lower motor neuron involvement, the search continues for a method that supports the diagnosis as high as EMG in the electrophysiological evaluation of upper motor neuron involvement. But it would be valuable to try to develop the standards of the classical transcranial cortical stimulation methods.

Methods:: Spinal and Cortical MEP responses and resting EDC, ADM, APB, AH, FCR, TA, and Soleus H reflex responses were recorded in the early period of 14 ALS patients according to the Revise El Escorial criteria. In addition, MScanMUNEs of the patients were calculated from APB and TA.

Results:: We investigated 14 patients with a mean age of 59.5±9.2 years, 3 of whom were female. Cortical stimulation failed to respond in 38% of APB, 38% of TA, and 54% of both TA and APB. The MScan MUNE of APB was 44±22. MScan MUNE of TA was 96±51. While soleus H reflex was obtained in 92% of the cases, H reflex response could be obtained in 27% of FCR, 17% of APB, AH, TA, and 8% of EDC and ADM. MScan MUNE values in 4 cases with normal TCCS and H reflex findings were lower than normal for APB.

Conclusions:: While MEP responses can be obtained from APB and TA with spinal stimulation, we believe that the inability to obtain MEP responses with cortical stimulation may be a biomarker in demonstrating upper motor neuron involvement with early-stage ALS cases.
THE EPSILON (EARLY PARKINSON WITH L-DOPA/DDCI AND OPICAPONE) STUDY IN EARLY PARKINSON’S DISEASE: DESIGN AND RATIONALE OF A PHASE III, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDY

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Background and Aims:: Opicapone (OPC) proved to be effective in the treatment of end-of-dose motor fluctuations in Parkinson’s disease (PD) patients. When OPC is co-administered with levodopa (L-dopa) and dopa decarboxylase inhibitor (DDCis), peripheral catechol-O-methyltransferase (COMT) is inhibited which increases L-dopa bioavailability. This study aims to explore the potential of OPC to enhance the clinical benefit of L-dopa/DDCi in patients with early-stage PD on stable treatment.

Methods:: Patients (aged 30–80 years) with idiopathic PD, treated with 3-4 daily oral doses of up to 500 mg L-dopa, with signs of treatable motor disability but no motor complications will be randomized (1:1) to receive OPC 50mg once-daily or placebo during a 6-month double-blind evaluation period. The L-dopa/DDCi regimen should remain stable throughout the double-blind period. At the end of this period, patients may enter a 1-year, open-label period of OPC 50mg treatment (Figure 1); 162 patients in each group are necessary to detect a minimum clinically-relevant magnitude of effect between arms.

Results:: Change from baseline in the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III is the primary endpoint. Secondary endpoints include tolerability, functional motor and non-motor assessments (MDS-UPDRS, Non-Motor Symptoms Scale, Parkinson's Disease Questionnaire-39, Parkinson's Disease Sleep Scale-2), and global impression of change scales (Clinical-Global-Impression-of-Change, Patient-Global-Impression-of-Change). First-patient-in is expected for early 2021 and last-patient-out from double-blind period in late 2022. Timelines might be impacted by the COVID-19 pandemic situation.

Conclusions:: This study will evaluate the effect of OPC on motor symptoms when given as add-on to stable L-dopa/DDCi therapy in patients with early-stage PD.
ADOPTION (EARLY LEVODOPA WITH OPICAPONE IN PARKINSON’S PATIENTS WITH MOTOR FLUCTUATIONS) STUDY IN PARKINSON’S DISEASE: DESIGN AND RATIONALE OF A RANDOMIZED PROSPECTIVE, OPEN-LABEL EXPLORATORY TRIAL

Joaquim Ferreira¹, Werner Poewe², Olivier Rascol³, Fabrizio Stocchi⁴, Angelo Antonini⁵, Raquel Costa⁶, Diogo Magalhães⁶, José Rocha⁷, Patrício Soares-Da-Silva⁷
¹Faculty of Medicine, University of Lisbon, Laboratory Of Clinical Pharmacology And Therapeutics, Lisbon, Portugal, ²Medical University of Innsbruck, Department Of Neurology, Innsbruck, Austria, ³University of Toulouse, Department Of Neurosciences & Clinical Pharmacology, Toulouse, France, ⁴IRCCS San Raffaele Pisana, Department Of Neurology, Rome, Italy, ⁵University of Padova, Department Of Neurosciences, Padova, Italy, ⁶BIAL-Portela & Ca S.A., Research And Development Department, Coronado, Portugal, ⁷BIAL-Portela & Ca S.A., Global Parkinson’s Disease Department, Coronado, Portugal

Background and Aims:: Opicapone (OPC) proved to be effective in the treatment of end-of-dose motor fluctuations in Parkinson’s disease (PD) patients. About 80–100% of PD patients show some degree of wearing-off within 10 years of levodopa (L-dopa) therapy. Approaches to optimize the L-dopa regimen include increasing the dose or ‘fractionating’ the total daily dose. This study aims to explore the potential of adjunctive OPC versus an additional dose of L-dopa/dopa decarboxylase inhibitor (DDCi) to optimize the L-dopa/DDCi regimen as first-line approach to treat wearing-off.

Methods:: Approximately 100 patients (aged ≥30 years) with idiopathic PD, treated with 3–4 daily oral L-dopa doses up to 600 mg, and signs of wearing-off (<2 years) will be equally randomized to receive OPC 50 mg once daily or an additional dose of 100 mg/25 mg L-dopa/DDCi during a 4-week open-label evaluation period (Figure 1).

Results:: Primary endpoint is the change from baseline in OFF-time. Secondary endpoints include tolerability, functional motor and non-motor assessments (Movement Disorder Society (MDS)-Unified Parkinson’s Disease Rating Scale, MDS-Non-Motor Symptoms, Parkinson's Disease Questionnaire-8), and global impression of change scales (Clinical Global Impression of Change, Patient Global Impression of Change). As this is a descriptive/exploratory study, no formal sample size calculation was performed. Study sites are in Germany, Italy, Portugal, Spain, and the UK. First-patient-in is expected for 2021 and
last-patient-out for late 2022. Timelines might be impacted by the COVID-19 situation.

**Conclusions:** This study will evaluate the potential of adjunctive OPC versus an additional dose of L-dopa/DDCi as first-line approach to treat wearing-off in PD patients.
THE OCEAN (OPICAPONE EFFECT ON MOTOR FLUCTUATIONS AND ASSOCIATED PAIN) STUDY IN PARKINSON’S DISEASE: DESIGN AND RATIONALE OF A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

K Ray Chaudhuri¹, Per Odin², Joaquim Ferreira³, Angelo Antonini⁴, Olivier Rascol⁵, Mónica Kurtis⁶, Alexander Storch⁷, Kirsty Bannister⁸, Raquel Costa⁹, Diogo Magalhães¹⁰, José Rocha¹⁰, Patrício Soares-Da-Silva¹⁰

¹Psychology & Neuroscience at King’s College and Parkinson Foundation International Centre of Excellence at King’s College Hospital, Institute Of Psychiatry, London, United Kingdom, ²Lund University Hospital, Department Of Neurology, Lund, Sweden, ³Faculty of Medicine, University of Lisbon, Laboratory Of Clinical Pharmacology And Therapeutics, Lisbon, Portugal, ⁴University of Padova, Department Of Neurosciences, Padova, Italy, ⁵University of Toulouse, Department Of Neurosciences & Clinical Pharmacology, Toulouse, France, ⁶Functional Movement Disorders Unit, Hospital Ruber Internacional Madrid, Neurology Department, Madrid, Spain, ⁷University of Rostock, Department Of Neurology, Rostock, Germany, ⁸Guy’s Campus, King’s College London, Institute Of Psychiatry, Psychology And Neuroscience, London, United Kingdom, ⁹BIAL-Portela & Ca S.A., Research And Development Department, Coronado, Portugal, ¹⁰BIAL-Portela & Ca S.A., Global Parkinson’s Disease Department, Coronado, Portugal

Background and Aims:: Opicapone (OPC) proved to be effective in the treatment of end-of-dose motor fluctuations in Parkinson’s disease (PD) patients. End-of-dose motor fluctuations and associated pain are commonly observed in patients with PD receiving levodopa (L-dopa)/DOPA decarboxylase inhibitors (DDCI). Motor fluctuations have a detrimental impact on patients’ quality of life and are in part mediated via dopaminergic pathways. This study aims to evaluate if treatment with OPC can improve pain related to end-of-dose fluctuations, consequently improving patients’ well-being.

Methods:: Patients (≥30 years old) with idiopathic PD, who were treated with 3–8 daily oral doses of L-dopa/DDCI and experienced pain associated with ‘wearing-off’ (end-of-dose deterioration), will be randomized (1:1) to OPC 50 mg once daily or placebo during a 24-week evaluation period (Figure 1). To detect a minimum clinically-relevant magnitude of effect between arms, 70 patients per group are necessary.
**Results:** The primary endpoint is change from baseline in domain 3 (fluctuation-related pain) of the King’s-Parkinson’s-Disease-Pain-Scale (KPPS). Secondary endpoints include tolerability, functional motor and non-motor assessments (KPSS, Movement Disorder Society-Non-Motor Symptoms [NMS], Parkinson's Disease Questionnaire-8 [PDQ-8], Hauser's home diary), and global impression of change scales (Clinical Global Impression of Change [CGI-C], Patient Global Impression of Change [PGI-C]). Study sites are in Germany, Italy, Portugal, Spain, and the UK. First-patient-in is expected for 2021 and last-patient-out for late 2022. Timelines might be impacted by the COVID-19 pandemic situation.

**Conclusions:** This study will evaluate the impact of 50 mg OPC once daily as adjunctive therapy to L-dopa/DDCI on pain associated with motor fluctuations.
INFLUENCE OF ONSET OF MOTOR FLUCTUATIONS ON THE EFFECTIVENESS OF OPICAPONE IN PARKINSON’S DISEASE PATIENTS WITH MOTOR FLUCTUATIONS: FINDINGS FROM THE REAL-WORLD OPTIPARK STUDY

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Background and Aims:: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in patients with Parkinson’s disease (PD). The OPTIPARK study evaluated OPC 50 mg in a heterogeneous population of patients treated in real-world conditions. This post-hoc analysis evaluated the influence of the onset of motor fluctuations (OMF) on the response to OPC treatment in PD patients with MF.

Methods:: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. PD patients with MF received OPC 50 mg in addition to current antiparkinsonian treatment. The primary efficacy 3-month endpoint was Clinician’s-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient’s-Global-Impression-of-Change (PGI-C), 8-item PD-Questionnaire (PDQ-8), Unified PD Rating Scale (UPDRS), and Non-Motor Symptoms Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). The influence of OMF was evaluated for each outcome in patients who completed the study.

Results:: Overall, 393 (82.4%) patients completed the 3-month endpoint (completers-set, Table 1). Of these patients, those with an earlier OMF (>1 year) reported slightly greater improvements in perception on CGI-C and PGI-C compared with those with recent OMF (≤1 year) (Table 2). However, recent fluctuators experienced greater improvements on UPDRS-II, quality-of-life (PDQ-8), and non-motor symptoms (NMSS); no difference was observed for UPDRS-III (Table 3). Furthermore, the incidence of TEAEs considered at least possibly related to OPC was also lower for recent fluctuators (Table 3).

<table>
<thead>
<tr>
<th>Table 1. Baseline characteristics (Completers-Set)</th>
</tr>
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<tbody>
<tr>
<td>Category</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
</tr>
<tr>
<td>Male, n (%)</td>
</tr>
<tr>
<td>Male, n (%)</td>
</tr>
<tr>
<td>PD duration, mean (SD) years</td>
</tr>
<tr>
<td>Onset of MF, mean (SD) years</td>
</tr>
<tr>
<td>L-dopa amount, mean (SD) mg</td>
</tr>
<tr>
<td>L-dopa, levodopa, MF, motor fluctuations, OMF, onset of MF, PD, Parkinson’s Disease, SD, standard deviation</td>
</tr>
</tbody>
</table>
Conclusions:: Overall, these findings indicate that patients with recent OMF may benefit at least as much as patients with earlier OMF from using OPC 50 mg as adjunctive therapy to levodopa.
INFLUENCE OF LEVODOPA DAILY DOSE ON THE EFFECTIVENESS OF OPICAPONE IN PARKINSON’S DISEASE PATIENTS WITH MOTOR FLUCTUATIONS: FINDINGS FROM THE REAL-WORLD OPTIPARK STUDY

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Background and Aims:: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson’s disease (PD) patients. The OPTIPARK study evaluated OPC 50mg in a heterogeneous population of patients treated in real-world conditions. We evaluated the influence of levodopa daily dose at baseline on the response to OPC in PD patients with MF.

Methods:: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. PD patients with MF received OPC 50mg in addition to current antiparkinsonian treatment. The primary efficacy 3-month endpoint was Clinician’s-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient’s-Global-Impression-of-Change (PGI-C), quality of life (8-item PD Questionnaire [PDQ-8]), Unified-PD-Rating-Scale (UPDRS), and Non-Motor-Symptoms-Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated the influence of levodopa daily dose at baseline in patients who completed the study for each outcome.

Results:: 393 (82.4%) patients completed the 3-month endpoint (completers-set, Table 1). A greater proportion of patients taking ‘low-levodopa’ daily dose experienced ‘very-much/much improvement’ on CGI-C and PGI-C scales when compared with patients taking ‘high-levodopa’ daily dose (Table 2). Similarly, patients taking ‘low-levodopa’ daily dose reported greater improvements on both UPDRS-II and III, quality-of-life (PDQ-8), and non-motor-symptoms (NMSS) (Table 3). Lower incidence of TEAEs considered at least possibly related to OPC were also reported for patients taking ‘low-levodopa’ daily dose (Table 3).

Table 1. Baseline characteristics (Completers-Set)

<table>
<thead>
<tr>
<th>Category</th>
<th>&lt; 500 mg</th>
<th>≥ 500 mg</th>
<th>&lt; 750 mg</th>
<th>≥ 750 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>157</td>
<td>236</td>
<td>311</td>
<td>82</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>66.9 (9.4)</td>
<td>67.4 (8.8)</td>
<td>67.1 (9.2)</td>
<td>67.5 (8.4)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>88 (56.1)</td>
<td>169 (71.6)</td>
<td>194 (62.4)</td>
<td>63 (76.8)</td>
</tr>
<tr>
<td>PD duration, mean (SD)</td>
<td>7.5 (4.5)</td>
<td>9.0 (4.6)</td>
<td>8.1 (4.6)</td>
<td>9.5 (4.5)</td>
</tr>
<tr>
<td>Onset of MF, mean (SD)</td>
<td>2.1 (3.3)</td>
<td>2.6 (2.8)</td>
<td>2.1 (2.9)</td>
<td>3.3 (3.1)</td>
</tr>
<tr>
<td>L-dopa amount, mean (SD)</td>
<td>330 (90)</td>
<td>710 (196)</td>
<td>461 (156)</td>
<td>927 (164)</td>
</tr>
</tbody>
</table>

L-dopa, levodopa; MF, motor fluctuations; PD, Parkinson’s disease; SD, standard deviation
Conclusions: These findings indicate that patients with PD and MF who receive ‘low-levodopa’ daily dose (representative of recent fluctuators) may have an added benefit from using OPC 50mg as adjunctive therapy to levodopa.

Table 2. CGI-C and PGI-C results after 3 months (Completers-Set)

<table>
<thead>
<tr>
<th>Category</th>
<th>&lt; 500 mg</th>
<th>≥ 500 mg</th>
<th>&lt; 750 mg</th>
<th>≥ 750 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGI-C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not assessed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very much improved</td>
<td>12 (7.6)</td>
<td>18 (7.6)</td>
<td>25 (8.0)</td>
<td>5 (6.1)</td>
</tr>
<tr>
<td>Much improved</td>
<td>71 (45.2)</td>
<td>96 (40.7)</td>
<td>139 (44.4)</td>
<td>28 (34.1)</td>
</tr>
<tr>
<td>Minimally improved</td>
<td>49 (31.2)</td>
<td>74 (31.4)</td>
<td>90 (28.9)</td>
<td>33 (40.2)</td>
</tr>
<tr>
<td>No change</td>
<td>21 (13.4)</td>
<td>35 (14.8)</td>
<td>41 (13.2)</td>
<td>15 (18.3)</td>
</tr>
<tr>
<td>Minimally worse</td>
<td>3 (1.9)</td>
<td>10 (4.2)</td>
<td>12 (3.9)</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>Much worse</td>
<td>1 (0.6)</td>
<td>2 (0.8)</td>
<td>3 (1.0)</td>
<td>-</td>
</tr>
<tr>
<td>Very much worse</td>
<td>-</td>
<td>1 (0.4)</td>
<td>1 (0.3)</td>
<td>-</td>
</tr>
<tr>
<td>PGI-C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not assessed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very much improved</td>
<td>12 (7.6)</td>
<td>18 (7.6)</td>
<td>26 (8.4)</td>
<td>4 (4.9)</td>
</tr>
<tr>
<td>Much improved</td>
<td>73 (46.5)</td>
<td>86 (36.4)</td>
<td>131 (42.1)</td>
<td>28 (34.1)</td>
</tr>
<tr>
<td>Minimally improved</td>
<td>41 (26.1)</td>
<td>72 (30.5)</td>
<td>84 (27.0)</td>
<td>29 (35.4)</td>
</tr>
<tr>
<td>No change</td>
<td>23 (14.6)</td>
<td>35 (14.8)</td>
<td>46 (14.8)</td>
<td>12 (14.6)</td>
</tr>
<tr>
<td>Minimally worse</td>
<td>6 (3.8)</td>
<td>19 (8.1)</td>
<td>19 (6.1)</td>
<td>6 (7.3)</td>
</tr>
<tr>
<td>Much worse</td>
<td>2 (1.3)</td>
<td>4 (1.7)</td>
<td>4 (1.3)</td>
<td>2 (2.4)</td>
</tr>
<tr>
<td>Very much worse</td>
<td>-</td>
<td>2 (0.8)</td>
<td>1 (0.3)</td>
<td>1 (1.2)</td>
</tr>
</tbody>
</table>

CGI-C, Clinician’s Global Impression of Change; PGI-C, Patient’s Global Impression of Change

Table 3. Secondary, after 3 months, and safety outcomes (Completers-Set)

<table>
<thead>
<tr>
<th>Category</th>
<th>&lt; 500 mg</th>
<th>≥ 500 mg</th>
<th>&lt; 750 mg</th>
<th>≥ 750 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>UPDRS II (at ON stage)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;.0001</td>
<td>&lt;.0001</td>
<td>&lt;.0001</td>
<td>0.2983</td>
</tr>
<tr>
<td>UPDRS III</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;.0001</td>
<td>&lt;.0001</td>
<td>&lt;.0001</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>PDQ-8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;.0001</td>
<td>0.0008</td>
<td>&lt;.0001</td>
<td>0.0919</td>
</tr>
<tr>
<td>NMSS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;.0001</td>
<td>&lt;.0001</td>
<td>&lt;.0001</td>
<td>0.0561</td>
</tr>
<tr>
<td>Any TEAE, n (%)</td>
<td>97 (61.8)</td>
<td>184 (78.0)</td>
<td>210 (67.5)</td>
<td>71 (86.6)</td>
</tr>
<tr>
<td>At least possibly related TEAEs, n (%)</td>
<td>54 (34.4)</td>
<td>100 (42.4)</td>
<td>112 (36.0)</td>
<td>42 (51.2)</td>
</tr>
</tbody>
</table>
EFFECTIVENESS OF OPICAPONE IN PARKINSON’S DISEASE PATIENTS WITH MOTOR FLUCTUATIONS ACCORDING TO BASELINE USE OF SAFINAMIDE: FINDINGS FROM THE REAL-WORLD OPTIPARK STUDY

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¹Newcastle University, Institute Of Neuroscience, Newcastle upon Tyne, United Kingdom, ²National Hospital for Neurology and Neurosurgery, Department Of Clinical And Movement Neurosciences, London, United Kingdom, ³University of Dresden, Department Of Neurology, Dresden, Germany, ⁴BIAL-Portela & Ca S.A., Global Parkinson’s Disease Department, Coronado, Portugal

Background and Aims:: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson’s disease (PD) patients. The OPTIPARK study evaluated OPC 50 mg in a heterogeneous population of patients treated in real-world conditions. We evaluated the effectiveness of OPC in PD patients with MF according to baseline use of safinamide (SAF).

Methods:: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. PD patients with MF received OPC 50 mg in addition to current antiparkinsonian treatment. Primary efficacy endpoint at 3 months was Clinician’s-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient’s-Global-Impression-of-Change (PGI-C), quality of life (8-item PD-Questionnaire [PDQ-8]), Unified PD Rating Scale (UPDRS) and Non-Motor Symptoms Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated the influence of baseline use of SAF in patients who completed the study for each outcome.

Results:: Overall, 393 (82.4%) patients completed the 3-month endpoint (completers-set, Table 1). Of these, patients not using SAF at baseline experienced greater improvements on CGI-C and PGI-C, when compared to patients using SAF at baseline (Table 2). Except for PDQ-8, patients using SAF at baseline experienced greater improvements on UPDRS-II and III, and non-motor symptoms (NMSS), when compared to patients not using SAF at baseline (Table 3). Similar incidence of TEAEs considered at least possibly related to OPC were reported for both subgroups (Table 3).

| Table 1. Baseline characteristics (Completers-Set) |
|---------------------------------|-------------------------------|-------------------------------|
| Category                        | Used SAF at Baseline          | Not Used SAF at Baseline      |
|                                 | N=53                          | N=340                         |
| Age, mean (SD)                  | 66.6 (9.2)                    | 67.2 (9.1)                    |
| Male, n (%)                     | 40 (75.5)                     | 217 (63.8)                    |
| PD duration, mean (SD) years    | 8.3 (4.3)                     | 8.4 (4.7)                     |
| Onset of MF, mean (SD) years    | 2.6 (3.2)                     | 2.4 (3.0)                     |
| L-dopa amount, mean (SD) mg     | 572 (223)                     | 556 (251)                     |
| L-dopa, levodopa, MF, motor fluctuations; PD, Parkinson’s Disease; SAF, safinamide; SD, standard deviation; |
Conclusions:: Overall, these findings indicate that patients may benefit from using OPC 50 mg with or without safinamide as adjunctive therapy to levodopa.
Background and Aims:: Opicapone (OPC), a once-daily catechol-O-methyltransferase inhibitor, proved to be effective in treating end-of-dose motor fluctuations in Parkinson’s disease (PD) patients in two large multinational trials. The OPTIPARK study evaluated OPC 50 mg in a heterogeneous population of PD patients treated in real-world conditions.

Methods:: OPTIPARK was a prospective, open-label, single-arm, multicenter trial conducted in Germany and the UK. PD patients with motor fluctuations received OPC 50 mg in addition to current antiparkinsonian treatment. Primary efficacy endpoint was Clinician’s Global Impression of Change (CGI-C) after 3 months. Secondary efficacy endpoints included Patient’s Global Impression of Change (PGI-C) and Unified Parkinson’s Disease Rating Scale (UPDRS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). Here UK-only data are reported.

Results:: A total of 132 patients took ≥1 OPC dose (Safety Set; Table 1) and 102 completed the 3-month treatment. Of 128 patients with post-baseline efficacy data (Full Analysis Set), 72.7% and 78.4% experienced any (very much/much/minimal) improvement on CGI-C and PGI-C after 3 months, respectively (Table 2). There were relevant improvements on UPDRS II and III scores (Table 3). TEAEs considered at least possibly related to OPC were reported for 65.2% of patients, the most frequently reported being dyskinesia (27.3%) and dry mouth (12.1%); 87.8% of TEAEs were of mild or moderate intensity. Serious TEAEs considered at least possibly related to OPC were reported for two (1.5%) patients.

Table 1. Baseline characteristics (Safety Set)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=132</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender, n (%)</td>
<td>81 (61.4)</td>
</tr>
<tr>
<td>Age, mean (SD) years</td>
<td>67.3 (8.4)</td>
</tr>
<tr>
<td>Disease duration, mean (SD) years</td>
<td>8.9 (5.2)</td>
</tr>
<tr>
<td>Duration of motor fluctuations, mean (SD) years</td>
<td>2.6 (2.8)</td>
</tr>
<tr>
<td>SD, standard deviation</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. CGI-C and PGI-C results after 3 months (Full Analysis Set)

<table>
<thead>
<tr>
<th>Category</th>
<th>CGI-C N=128</th>
<th>PGI-C N=102</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not assessed</td>
<td>1 (0.8)</td>
<td>0</td>
</tr>
<tr>
<td>Very much improved</td>
<td>15 (11.7)</td>
<td>14 (13.7)</td>
</tr>
<tr>
<td>Much improved</td>
<td>47 (36.7)</td>
<td>39 (38.2)</td>
</tr>
<tr>
<td>Minimally improved</td>
<td>31 (24.2)</td>
<td>27 (26.5)</td>
</tr>
<tr>
<td>No change</td>
<td>22 (17.2)</td>
<td>9 (8.8)</td>
</tr>
<tr>
<td>Minimally worse</td>
<td>5 (3.9)</td>
<td>10 (9.8)</td>
</tr>
<tr>
<td>Much worse</td>
<td>5 (3.9)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Very much worse</td>
<td>2 (1.6)</td>
<td>2 (2.0)</td>
</tr>
</tbody>
</table>

LOCF applied to CGI-C

CGI-C, Clinician’s Global Impression of Change; LOCF, Last Observation Carried Forward; PGI-C, Patient’s Global Impression of Change
**Table 3. Changes from baseline in UPDRS scores (Full Analysis Set)**

<table>
<thead>
<tr>
<th>Scale</th>
<th>N</th>
<th>Mean (SD) change from baseline to 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>UPDRS II (activities of daily living) score at OFF stage</td>
<td>101</td>
<td>-2.2 (4.9)</td>
</tr>
<tr>
<td>UPDRS II (activities of daily living) score plus III (motor function) score at ON stage</td>
<td>102</td>
<td>-3.7 (10.7)</td>
</tr>
<tr>
<td>UPDRS III (motor function) score at ON stage</td>
<td>100</td>
<td>-2.7 (8.3)</td>
</tr>
</tbody>
</table>

SD, standard deviation; UPDRS, Unified Parkinson’s Disease Rating Scale

**Conclusions:** OPC 50 mg was effective and generally well tolerated in UK PD patients with motor fluctuations treated in clinical practice.
OPICAPONE IN CLINICAL PRACTICE IN PARKINSON’S DISEASE GERMAN PATIENTS WITH MOTOR FLUCTUATIONS: FINDINGS FROM THE OPTIPARK STUDY

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1University of Dresden, Department Of Neurology, Dresden, Germany, 2National Hospital for Neurology and Neurosurgery, Department Of Clinical And Movement Neurosciences, London, United Kingdom, 3BIAL-Portela & Ca S.A., Global Parkinson’s Disease Department, Coronado, Portugal

Background and Aims:: Opicapone (OPC), a once-daily catechol-O-methyltransferase inhibitor, proved to be effective in treating end-of-dose motor fluctuations in Parkinson’s disease (PD) patients in two large multinational trials. The OPTIPARK study evaluated OPC 50 mg when used in a heterogeneous population of PD patients with motor fluctuations treated in real-world conditions.

Methods:: OPTIPARK was a prospective, open-label, single-arm, multicenter trial conducted in Germany and the UK. Patients with motor fluctuations received OPC 50 mg in addition to current antiparkinsonian treatment. Primary efficacy endpoint was Clinician’s Global Impression of Change (CGI-C) after 3 months. Secondary efficacy endpoints included Patient’s Global Impression of Change (PGI-C) and Unified Parkinson’s Disease Rating Scale (UPDRS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). Here Germany-only data are reported.

Results:: In total, 363 patients took ≥1 OPC dose (Safety Set; Table 1) and 291 completed the 3-month treatment. Of 349 patients with post-baseline efficacy data (Full Analysis Set), 70.8% and 76.3% experienced any (very much/much/minimal) improvement on CGI-C and PGI-C after 3 months, respectively (Table 2). There were relevant improvements on UPDRS II and III scores (Table 3). TEAEs considered at least possibly related to OPC were reported for 37.7% of patients, the most frequently reported being dyskinesia (5.8%) and dry mouth (4.4%); 91.7% of TEAEs were of mild or moderate intensity. Serious TEAEs considered at least possibly related to OPC were reported for five (1.4%) patients.

<table>
<thead>
<tr>
<th>Table 1. Baseline characteristics (Safety Set)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>N=363</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
</tr>
<tr>
<td>Age, mean (SD) years</td>
</tr>
<tr>
<td>Disease duration, mean (SD) years</td>
</tr>
<tr>
<td>Duration of motor fluctuations, mean (SD) years</td>
</tr>
<tr>
<td>SD, standard deviation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. CGI-C and PGI-C results after 3 months (Full Analysis Set)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category                                CGI-C</td>
</tr>
<tr>
<td>N=349</td>
</tr>
<tr>
<td>Not assessed                             2 (0.6)</td>
</tr>
<tr>
<td>Very much improved                      16 (4.6)</td>
</tr>
<tr>
<td>Much improved                           127 (36.4)</td>
</tr>
<tr>
<td>Minimally improved                     104 (29.8)</td>
</tr>
<tr>
<td>No change                              66 (18.9)</td>
</tr>
<tr>
<td>Minimally worse                         23 (6.6)</td>
</tr>
<tr>
<td>Much worse                             10 (2.9)</td>
</tr>
<tr>
<td>Very much worse                        1 (0.3)</td>
</tr>
<tr>
<td>LOCF applied to CGI-C</td>
</tr>
</tbody>
</table>

CGI-C, Clinician’s Global Impression of Change; LOCF, Last Observation Carried Forward; PGI-C, Patient’s Global Impression of Change.
Conclusions: OPC 50 mg was effective and generally well tolerated in German PD patients with motor fluctuations treated in clinical practice.
THE OASIS (OPICAPONE IN SLEEP DISORDER) STUDY IN PARKINSON’S DISEASE: DESIGN AND RATIONALE OF AN OPEN-LABEL, SINGLE-ARM, PILOT TRIAL

Raquel Costa1, Claudia Trenkwalder2, Joaquim Ferreira3, Diogo Magalhães4, José Rocha4, Patrício Soares-Da-Silva4
1BIAL-Portela & Ca S.A., Research And Development Department, Coronado, Portugal, 2Paracelsus-Elena Klinik, Neurology Department, Kassel, Germany, 3Faculty of Medicine, University of Lisbon, Laboratory Of Clinical Pharmacology And Therapeutics, Lisbon, Portugal, 4BIAL-Portela & Ca S.A., Global Parkinson’s Disease Department, Coronado, Portugal

Background and Aims:: Opicapone (OPC) proved to be effective in the treatment of end-of-dose motor fluctuations in Parkinson’s disease (PD) patients. Non-motor symptoms have a substantial impact on health-related quality of life and are reported in approximately 90% of idiopathic PD patients. End-of-dose motor fluctuations and associated sleep disorders are commonly observed in PD patients who receive treatment with levodopa (L-dopa)/DOPA decarboxylase inhibitors (DDCI). This study aims to evaluate the effects of OPC treatment on sleep disorders in PD patients with ‘wearing-off’.

Methods:: Approximately 30 patients (aged ≥30 years) with idiopathic PD, treated with 3–8 daily doses of L-dopa/DDCI, with ‘wearing-off’ and sleep disorders will receive OPC 50mg once daily during a 6-week evaluation period. L-dopa/DDCI daily dose, but not number of intakes, may be adjusted according to the patients’ response in the first 2 weeks, and is kept unchanged afterwards (Figure 1). As a pilot study, no formal sample size calculation was performed.

Results:: The primary endpoint is change from baseline in total score of Parkinson’s Disease Sleep Scale-2. Secondary endpoints include tolerability, functional motor and non-motor assessments (Movement Disorder Society-Non-Motor Symptoms Scale, Parkinson’s Disease Questionnaire-8, Parkinson’s Fatigue Scale, ON/OFF home diary), and Clinical and Patient Global Impression of Change scales. Study sites are in Germany and Portugal. First-patient-in is expected for early 2021 and last-
patient-out for late 2021. Timelines might be impacted by the COVID-19 situation.

**Conclusions:** This pilot study will provide preliminary data on the potential effect of OPC 50mg once daily as adjunctive therapy to L-dopa/DDCI on PD-associated sleep disorders.
INFLUENCE OF DEMOGRAPHIC CHARACTERISTICS ON THE EFFECTIVENESS OF OPICAPONE IN PARKINSON’S DISEASE PATIENTS WITH MOTOR FLUCTUATIONS: FINDINGS FROM THE REAL-WORLD OPTIPARK STUDY

Biju Mohamed¹, Andrew Lees², Heinz Reichmann³, Diogo Martins⁴, Diogo Magalhães⁴, José Rocha⁴, Patrício Soares-Da-Silva⁴
¹Cardiff and Vale University Health Board, Parkinson’s Specialist Service, Cardiff, United Kingdom, ²National Hospital for Neurology and Neurosurgery, Department Of Clinical And Movement Neurosciences, London, United Kingdom, ³University of Dresden, Department Of Neurology, Dresden, Germany, ⁴BIAL-Portela & Ca S.A., Global Parkinson’s Disease Department, Coronado, Portugal

Background and Aims:: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson’s disease (PD) patients. The OPTIPARK study evaluated OPC 50mg in a heterogeneous population of PD patients treated in real-world conditions. We evaluated the influence of baseline demographic characteristics on the response to OPC in PD patients with MF.

Methods:: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. PD patients with MF received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy endpoint at 3 months was Clinician’s-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient’s-Global-Impression-of-Change (PGI-C), 8-item PD Questionnaire (PDQ-8), Unified PD Rating (UPDRS) and Non-Motor Symptoms (NMSS) scales. Safety assessments included evaluation of treatment-emergent adverse-events (TEAEs). This post-hoc analysis evaluated the influence of demographic characteristics (i.e., age and gender) in patients who completed the study for each outcome.

Results:: Overall, 393 (82.4%) patients completed the 3-month endpoint (completers-set, Table 1). A greater proportion of younger (<67.2 years-old) and female patients experienced ‘very much/much improvement’ on CGI-C and PGI-C when compared, respectively, to older and male patients (Table 2). Except for UPDRS-II, younger and male patients reported greater improvements on UPDRS-III, PDQ-8 and NMSS, when compared to older and female patients (Table 3). Lower incidence of TEAEs considered at least possibly related to OPC were reported for younger and male patients, when compared to older and female patients (Table 3).

<table>
<thead>
<tr>
<th>Table 1. Baseline characteristics (Completers-Set)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>N</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
</tr>
<tr>
<td>Male, n (%)</td>
</tr>
<tr>
<td>PD duration, mean (SD) years</td>
</tr>
<tr>
<td>Onset of MF, mean (SD) years</td>
</tr>
<tr>
<td>L-dopa amount, mean (SD) mg</td>
</tr>
</tbody>
</table>

*mean age at baseline
L-dopa, levodopa; MF, motor fluctuations; PD, Parkinson’s disease; SD, standard deviation
Conclusions: These findings indicate that younger PD patients with MF may have an added benefit from using OPC 50mg as adjunctive therapy to levodopa.
EFFECTIVENESS OF OPICAPONE IN PARKINSON’S DISEASE PATIENTS WITH MOTOR FLUCTUATIONS ACCORDING TO BASELINE USE OF DOPAMINE AGONISTS: FINDINGS FROM THE REAL-WORLD OPTIPARK STUDY

Wolfgang Jost¹, Heinz Reichmann², Andrew Lees³, Daniela Marinho⁴, Diogo Magalhães⁴, José Rocha⁴, Patrício Soares-Da-Silva⁴
¹Parkinson-Klinik Ortenau, Neurology Department, Wolfach, Germany, ²University of Dresden, Department Of Neurology, Dresden, Germany, ³National Hospital for Neurology and Neurosurgery, Department Of Clinical And Movement Neurosciences, London, United Kingdom, ⁴BIAL-Portela & Ca S.A., Global Parkinson’s Disease Department, Coronado, Portugal

Background and Aims:: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson’s disease (PD) patients. The OPTIPARK study evaluated OPC 50 mg in a heterogeneous population of PD patients treated in real-world conditions. We evaluated the effectiveness of OPC in PD patients with MF according to baseline use of dopamine agonists (DA).

Methods:: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. PD patients with MF received OPC 50 mg in addition to current antiparkinsonian treatment. Primary efficacy 3-month endpoint was Clinician’s-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient’s-Global-Impression-of-Change (PGI-C), 8-item PD-Questionnaire (PDQ-8), Unified PD Rating Scale (UPDRS) and Non-Motor Symptoms Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated the influence of DA use at baseline in patients who completed the study for each outcome.

Results:: Overall, 393 (82.4%) patients completed the 3-month endpoint (completers-set, Table 1). Of these, patients using DA at baseline experienced greater improvements on CGI-C and PGI-C, when compared to patients not using DA at baseline (Table 2). Except for UPDRS-II, patients using DA at baseline experienced greater improvements on UPDRS-III, quality of life (PDQ-8) and non-motor symptoms (NMSS), when compared to patients not using DA at baseline (Table 3). Lower incidence of TEAEs considered at least possibly related to OPC were also reported for patients using DA at baseline (Table 3).
Conclusions:: Overall, these findings indicate that patients may benefit from using OPC 50 mg with or without DA as adjunctive therapy to levodopa.
EFFECTIVENESS OF OPICAPONE IN PARKINSON’S DISEASE PATIENTS WITH MOTOR FLUCTUATIONS ACCORDING TO BASELINE USE OF MONOAMINE-OXIDASE-B INHIBITORS AND DOPAMINE AGONISTS: THE REAL-WORLD OPTIPARK STUDY

Heinz Reichmann1, Tobias Warnecke2, Andrew Lees3, Diogo Martins4, Diogo Magalhães4, José Rocha4, Patrício Soares-Da-Silva4
1University of Dresden, Department Of Neurology, Dresden, Germany, 2University of Muenster, Department Of Neurology, Münster, Germany, 3National Hospital for Neurology and Neurosurgery, Department Of Clinical And Movement Neurosciences, London, United Kingdom, 4BIAL-Portela & Ca S.A., Global Parkinson’s Disease Department, Coronado, Portugal

Background and Aims:: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson’s disease (PD) patients. The OPTIPARK study evaluated OPC 50 mg in a heterogeneous population of PD patients treated in real-world conditions. We evaluated the effectiveness of OPC in PD patients with MF according to baseline use of monoamine-oxidase-B inhibitors (MAO-Bi) and dopamine agonists (DA).

Methods:: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. PD patients with MF received OPC 50 mg in addition to current antiparkinsonian treatment. Primary efficacy 3-month endpoint was Clinician’s-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient’s-Global-Impression-of-Change (PGI-C), quality of life (8-item PD-Questionnaire [PDQ-8]), Unified PD Rating Scale (UPDRS) and Non-Motor Symptoms Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated the influence of baseline use of both MAO-Bi and DA in patients who completed the study for each outcome.

Results:: Overall, 393 (82.4%) patients completed the 3-month endpoint (completers-set, Table 1). Of these, patients using MAO-Bi/DA at baseline experienced greater improvements on CGI-C and PGI-C, when compared to patients not using MAO-Bi/DA at baseline (Table 2). Except for NMSS, patients not using MAO-Bi/DA at baseline experienced greater improvements on UPDRS-II and III and quality-of-life (PDQ-8) (Table 3). Lower incidence of TEAEs considered at least possibly related to OPC were also reported for patients using MAO-Bi/DA at baseline (Table 3).

<p>| Table 1. Baseline characteristics (Completers-Set) |
|---------------------------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Category</th>
<th>Used MAO-Bi &amp; DA at Baseline</th>
<th>Not Used MAO-Bi &amp; DA at Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=145</td>
<td>N=248</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>64.6 (9.1)</td>
<td>68.6 (8.8)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>92 (63.4)</td>
<td>165 (66.5)</td>
</tr>
<tr>
<td>PD duration, mean (SD) years</td>
<td>8.8 (4.4)</td>
<td>8.2 (4.8)</td>
</tr>
<tr>
<td>Onset of MF, mean (SD) years</td>
<td>2.3 (2.8)</td>
<td>2.5 (3.1)</td>
</tr>
<tr>
<td>L-dopa amount, mean (SD) mg</td>
<td>487 (220)</td>
<td>600 (253)</td>
</tr>
</tbody>
</table>

L-dopa, levodopa; MF, motor fluctuations; OMF, onset of MF; PD, Parkinson’s Disease; SD, standard deviation
Conclusions:: Overall, these findings indicate that patients may benefit from using OPC 50 mg with or without MAO-Bi/DA as adjunctive therapy to levodopa.

Table 2. CGI-C and PGI-C results after 3 months (Completers-Set)

<table>
<thead>
<tr>
<th>Category</th>
<th>Used MAO-Bi &amp; DA at Baseline</th>
<th>Not Used MAO-Bi &amp; DA at Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=145</td>
<td>N=748</td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>CGI-C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not assessed</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Very much improved</td>
<td>11 (7.6)</td>
<td>19 (7.7)</td>
</tr>
<tr>
<td>Much improved</td>
<td>67 (46.2)</td>
<td>100 (40.3)</td>
</tr>
<tr>
<td>Minimally improved</td>
<td>38 (26.2)</td>
<td>85 (34.3)</td>
</tr>
<tr>
<td>No change</td>
<td>20 (13.8)</td>
<td>36 (14.5)</td>
</tr>
<tr>
<td>Minimally worse</td>
<td>6 (4.1)</td>
<td>7 (2.8)</td>
</tr>
<tr>
<td>Much worse</td>
<td>2 (1.4)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Very much worse</td>
<td>1 (0.7)</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 3. Secondary, after 3 months, and safety outcomes (Completers-Set)

<table>
<thead>
<tr>
<th>Category</th>
<th>Used MAO-Bi &amp; DA at Baseline</th>
<th>Not Used MAO-Bi &amp; DA at Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=145</td>
<td>N=748</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>p-value</td>
</tr>
<tr>
<td>UPDRS II (at ON stage), mean (SD)</td>
<td>-1.5 (3.6)</td>
<td>-1.7 (3.8)</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>UPDRS III, mean (SD)</td>
<td>-4.3 (7.9)</td>
<td>-4.8 (8.2)</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>PDQ-8, mean (SD)</td>
<td>-2.8 (11.1)</td>
<td>-3.8 (13.7)</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>.0034</td>
</tr>
<tr>
<td>NMS, mean (SD)</td>
<td>-7.7 (19.6)</td>
<td>-6.3 (19.8)</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Any TEAE, n (%)</td>
<td>100 (69.0)</td>
<td>181 (73.0)</td>
</tr>
<tr>
<td>At least possibly related TEAEs, n (%)</td>
<td>52 (35.9)</td>
<td>102 (41.1)</td>
</tr>
</tbody>
</table>

*Relationship to study medication reported as ‘possible’, ‘probable’, ‘definite’ or missing; TEAEs with onset or worsening after first opicapone intake until study termination, either regularly or prematurely; p-values obtained through Student’s t-test for the change from baseline.

NMS, Non-Motor Symptoms Scale; OMF, onset of motor fluctuations; PDQ-8, 8-item Parkinson’s Disease Questionnaire; SD, standard deviation; TEAE, treatment-emergent adverse event; UPDRS, Unified Parkinson’s Disease Rating Scale.
ASSESSMENT OF NON-MOTOR AND AUTONOMIC SYMPTOMS IN WILSON’S DISEASE PATIENTS

Sandra Perillo, Gianluigi Palmieri, Carmen Dello Iacovo, Filomena Di Canio, Margherita Matarazzo, Fabiola Di Dato, Raffaele Iorio, Giuseppe De Michele, Giovanna De Michele, Anna De Rosa

1University of Naples Federico II, Department Of Neurosciences, Odontostomatological And Reproductive Sciences, Naples, Italy, 2University of Naples Federico II, Department Of Translational Medical Science, Naples, Italy, 3University of Naples Federico II, Department Of Translational Medical Science, Section Of Pediatrics, Naples, Italy

Background and Aims:: Wilson’s Disease (WD) is a genetic disorder caused by excessive copper deposition in liver, brain and other organs. The core neurological symptoms mainly consist of movement disorders, though non-motor symptoms (NMS) can occur in early stages of the disease. We aimed to assess whether NMS are more common in WD patients in comparison with healthy subjects and if they correlate with gravity and disease duration.

Methods:: Twenty-five patients with genetically-proven WD (11 F, 14 M) and 26 healthy controls (Ctrl; 13 F, 14 M) comparable for age and education were enrolled. Patients underwent neurological examination, whereas NMS were assessed using the following clinical scales: Minimental State Examination (MMSE), SCOPA-AUT Questionnaire, Apathy Evaluation Scale (AES), Non-Motor Symptoms Scale (NMSS), Questionnaire for Impulsive-Compulsive Disorders in Parkinson’s disease (QUIP-RS), Beck Depression Inventory (BDI), Epworth Sleepiness Scale (ESS), Restless Legs Syndrome Rating Scale (RLSRS).

Results:: We did not find any statistically significant difference between the two groups in the scores of BDI (p=0.955), SCOPA-AUT Questionnaire (p=0.500), QUIP-RS (p=0.789) and RLSRS (p=0.609). Although ESS (p=0.123) and NMSS (p=0.150) scores were comparable, patients more frequently complained excessive daytime sleepiness and cardiovascular NMS (80% vs 19%, p<0.01; 96% vs 73%, p=0.023). Furthermore, global cognitive abilities assessed by MMSE were more impaired among patients, in particular in those with neurological disorders (p<0.001). Finally, disease duration positively correlated with AES scores (p= 0.032).

Conclusions:: Our study suggests that WD patients might more frequently show cognitive impairment and NMS, though these findings should be further investigated to improve disease management and diagnosis.
SUCCESSFUL TREATMENT OF PAROXYSMAL PAINFUL TONIC SPASMS WITH CARBAMAZEPINE IN A PATIENT WITH HYPERTROPHIC OLIVARY DEGENERATION

Alessia Fiore, Pietro Anceschi, Stefania Lazzari, Irene Florindo, Lucia Zinno, Antonio Pavarani, Elisabetta Chierici, Giovanni Pavesi

1Neurosciences Unit, Department Of Medicine And Surgery, University Of Parma, Parma, Italy, 2Neuroradiology Unit, Department Of Diagnostic, Parma University Hospital, Parma, Italy

Background and Aims:: Hypertrophic olivary degeneration (HOD) is a rare phenomenon that can occur after different insults to the so-called Guillain-Mollaret triangle. Clinically, HOD presents as palatal tremor, dentatorubral tremor and/or ocular myoclonus.

Methods:: We report the case of a 75-years-old female patient with a sudden-onset of stereotypical recurrent painful tonic spasms of the left limbs, with dystonic posture, lasting 10-20 seconds, without impairment of consciousness. We performed EEG, neurophysiological tests and Diffusion MRI tensor tractography.

Results:: Inter-ictal neurological examination displayed nistagmus and left Babinski sign. EEG did not show any epileptiform activity during the episodes. Brain MRI revealed a cavernoma in the left cerebellar cortex surrounded by edema and hypertrophy of the right olive with increased T2-signal intensity, suggestive of HOD. Motor evoked potentials showed prolonged central conduction time with low-amplitude responses on the left upper limb. Diffusion tensor tractography showed thinning of the right corticospinal tract compared to the controlateral side. Treatment with carbamazepine, 200 mg two times daily, led to the prompt resolution of the spasms.
Conclusions:: Dystonia in HOD has already been reported in literature with uncertain pathogenesis. Painful tonic spasms as a result of pyramidal tracts dysfunction have been described in demyelinating and vascular diseases. In this case, therapeutic response to carbamazepine, painfulness and shortness of the attacks, clinical and instrumental evidence of pyramidal involvement suggest a diagnosis of painful tonic spasms, more than dystonia. Corticospinal tract lesion could be hypothesized in the medulla oblongata, above pyramidal decussation, near HOD.
RELATIONSHIP BETWEEN CLINICAL SYMPTOMS AND AGEING, PARKINSON DISEASE

Bayasgalan Dagvadorj¹, Altantsetseg Purvee², Boloroo Sukhbaatar³
¹Bayangol District’s Health Center, Ulaanbaatar, Mongolia, Neurology, ulaanbaatar, Mongolia, ²The third central hospital, Neurology, ulaanbaatar, Mongolia, ³Zint clinic, Neurology, ulaanbaatar, Mongolia

Background and Aims:: Background: Ageing remains the biggest risk factor for developing idiopathic Parkinson’s disease (PD).

Methods:: This retrospective survey’s data were obtained from the PD database of the neurology clinics at tertiary care hospitals from January 1, 2017 to March 31, 2020.

Results:: 84 patients with PD (Female 80.6%), mean age 65.7±7.4. The age groups of the patients were 21.8% in middle age, 78.2% old age, while young is not. The duration of the disease after the diagnosis was compared with the Hoehn and Yahr stage, these duration in second stage 1.7±0.9 years; in third stage 5.7±2.8 years; in fourth stage 8.8±1.8 years; in fifth stage 11.4±3.9 years, respectively (p<0.01). Young-onset patients showed significantly longer duration to reach Stage IV, and V but shorter duration to develop wearing off and dyskinesia. In our study PD firstly diagnosed age was 59.4±8.8, in other studies has found similar result that the prodromal stage of PD coincides with midlife. If diagnosed age was young, Hoehn and Yahr stage was increased (p=0.01), (Table 1). Table.1 Hoehn and Yahr stage

<table>
<thead>
<tr>
<th>Firstly diagnosed age</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Middle age between 40-59</td>
<td>17.8%</td>
<td>51.4%</td>
<td>41.4%</td>
<td>100.0%</td>
<td>44.8%</td>
</tr>
<tr>
<td>Old age more than 60</td>
<td>82.2%</td>
<td>48.6%</td>
<td>58.6%</td>
<td>0.0%</td>
<td>55.2%</td>
</tr>
<tr>
<td>Total</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Conclusions:: Conclusion: Hoehn and Yahr transition time is a useful measure of disease progression in PD and may be used in clinical studies evaluating therapeutic interventions and prognostic factors in PD.
IMPACT OF COVID-19 ON ESSENTIAL TREMOR AND DYSTONIC TREMOR: EXPERIENCE OF AN ITALIAN CENTRE

Sandy Cartella, Carmen Terranova, Ignazio Arena, Angelo Quartarone, Paolo Girlanda
University of Messina, Department Of Clinical And Experimental Medicine, Messina, Italy

Background and Aims:: Covid-19 had a negative impact on movement disorders, but there are no studies on tremor. The only present studies regard the management of DBS and botulinum toxin. Our aim is to assess the impact of Covid-19 on Essential and Dystonic Tremor, with regard on non-motor symptoms and everyday life.

Methods:: Self-administered survey, based on Hamilton Depression and Anxiety Rating Scale, SARA, Hospital Anxiety and Depression Scale. Motor evaluation (TETRAS) before and after lockdown.

Results:: We analysed 26 patients. Depression worsened in 57,7% of them, anxiety in 26,9% and sleep quality in 34,6%. All these features are related between them and with the patient’s level of education, higher in those who felt more depressed, anxious and had a worsened sleep quality. 19,2% of patients felt their difficulty in concentration increased during lockdown. This is related to the increase in anxiety. None of the features is related to TETRAS score or to years of age or of disease. 38,4% of patients know what telemedicine is, 15,3% used it for a teleconsultation. 42,3% said quality of life worsened. 15,3% managed to practice physiotherapy during lockdown. Only one patient followed a physiotherapy video lesson. For most patients the major problems were the impossibility to go to the hospital and lack of social relationships. Most people emailed our centre to postpone appointments or to seek medical advice, only 1% for Covid-19 related issues and telemedicine consultations.

Conclusions:: Covid-19 had a negative direct impact on non-motor symptoms of ET and DT and an indirect one, with quality of life repercussions.
STUDY DESIGN TO ASSESS THE EFFECT OF OPICAPONE ON LEVODOPA PHARMACOKINETICS IN DIFFERENT LEVODOPA-OPTIMIZED TREATMENT REGIMENS IN PARKINSON’S DISEASE PATIENTS

Joaquim Ferreira1, Werner Poewe2, Olivier Rascol3, Fabrizio Stocchi4, Angelo Antonini5, Joana Moreira6, José Rocha6, Patrício Soares-Da-Silva6
1Faculty of Medicine, University of Lisbon, Laboratory Of Clinical Pharmacology And Therapeutics, Lisbon, Portugal, 2Medical University of Innsbruck, Department Of Neurology, Innsbruck, Austria, 3University of Toulouse, Department Of Neurosciences & Clinical Pharmacology, Toulouse, France, 4IRCCS San Raffaele Pisana, Department Of Neurology, Rome, Italy, 5University of Padova, Department Of Neurosciences, Padova, Italy, 6BIAL-Portela & Ca S.A., Global Parkinson’s Disease Department, Coronado, Portugal

Background and Aims:: Opicapone (OPC) is a catechol-O-methyltransferase inhibitor with proven efficacy in the treatment of end-of-dose motor fluctuations in Parkinson’s disease (PD) patients. Levodopa (LD) is considered the gold standard treatment of PD, yet comes with side effects including motor fluctuations and dyskinesia. Therefore, many physicians follow an LD-optimization strategy. This study was designed to assess the effect of OPC 50 mg once daily on LD pharmacokinetics (PK) in different LD/carbidopa (CD) treatment-optimized regimens in PD patients with end-of-dose motor fluctuations.

Methods:: 24 medically stable adult PD patients with a total daily LD/CD dose of 500/125 mg (preferably administered 5 times per day [Q5]) will be enrolled. From enrolment up to 14±2 days, an LD/CD-reference treatment of 100/25 mg LD/CD Q5 (500/125 mg total daily dose) will be administered. At baseline, patients will be equally randomized to: Q4 LD/CD-regimen of 400/100 mg total daily dose plus OPC 50mg Q5 LD/CD-regimen of 400/100 mg total daily dose plus OPC 50mg Patients will maintain the LD/CD+OPC regimens for up to 14±2 days. PK assessments for LD/CD-reference will be performed at V3 and V4 for both LD/CD+OPC regimens (Figure 1).

Results:: The primary endpoint will be PK based. Secondary endpoints include tolerability, functional motor assessments (subject diary charts for ON/OFF periods), and Patient Global Impression of Change scale (PGI-C). First-patient-in and last-patient-out are expected in 2021. Timelines might be impacted by the COVID-19 situation.
Conclusions:: This study will evaluate the effect of OPC on LD PK in different LD/CD treatment-optimized regimens in PD patients with end-of-dose motor fluctuations.
EFFECTIVENESS OF OPICAPONE IN PARKINSON’S DISEASE PATIENTS WITH MOTOR FLUCTUATIONS ACCORDING TO BASELINE USE OF ENTACAPONE: FINDINGS FROM THE REAL-WORLD OPTIPARK STUDY

Wolfgang Jost¹, Heinz Reichmann², Andrew Lees³, Daniela Marinho⁴, Diogo Magalhães⁴, José Rocha⁴, Patrício Soares-Da-Silva⁴
¹Parkinson-Klinik Ortenau, Neurology Department, Wolfach, Germany, ²University of Dresden, Department Of Neurology, Dresden, Germany, ³National Hospital for Neurology and Neurosurgery, Department Of Clinical And Movement Neurosciences, London, United Kingdom, ⁴BIAL-Portela & Ca S.A., Global Parkinson’s Disease Department, Coronado, Portugal

Background and Aims: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson’s disease (PD) patients. The OPTIPARK study evaluated OPC 50 mg in a heterogeneous population of PD patients treated in real-world conditions. We evaluated the effectiveness of OPC in PD patients with MF according to baseline use of entacapone (ENT).

Methods: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. PD patients with MF received OPC 50 mg in addition to current antiparkinsonian treatment. Primary efficacy endpoint at 3 months was Clinician’s-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient’s-Global-Impression-of-Change (PGI-C), quality of life (8-item PD Questionnaire [PDQ-8]), Unified PD Rating Scale (UPDRS) and Non-Motor Symptoms Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated the influence of baseline use of ENT in patients who completed the study for each outcome.

Results: Overall, 393 (82.4%) patients completed the 3-month endpoint (completers-set, Table 1). Of these, patients not using ENT at baseline experienced greater improvements on CGI-C and PGI-C, UPDRS-II and III, quality of life (PDQ-8) and non-motor symptoms (NMSS), when compared to patients using ENT (and switched) at baseline (Table 2, Table 3). Similar incidence of TEAEs considered at least possibly related to OPC were reported for both subgroups (Table 3).

<table>
<thead>
<tr>
<th>Table 1. Baseline characteristics (Completers-Set)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
</tr>
<tr>
<td>Male, n (%)</td>
</tr>
<tr>
<td>PD duration, mean (SD) years</td>
</tr>
<tr>
<td>Onset of MF, mean (SD) years</td>
</tr>
<tr>
<td>L-dopa amount, mean (SD) mg</td>
</tr>
<tr>
<td>ENT, entacapone; L-dopa, levodopa; MF, motor fluctuations; PD, Parkinson’s Disease; SD, standard deviation</td>
</tr>
</tbody>
</table>
Conclusions: Overall, these findings suggest that patients might benefit from receiving OPC as first catechol-O-methyl transferase inhibitor as adjunctive therapy to levodopa.
INFLUENCE OF DISEASE DURATION ON THE EFFECTIVENESS OF OPICAPONE IN PARKINSON’S DISEASE PATIENTS WITH MOTOR FLUCTUATIONS: FINDINGS FROM THE REAL-WORLD OPTIPARK STUDY

Tobias Warnecke¹, Heinz Reichmann², Andrew Lees³, Daniela Marinho⁴, Diogo Magalhães⁴, José Rocha⁴, Patrício Soares-Da-Silva⁴
¹University of Muenster, Department Of Neurology, Münster, Germany, ²University of Dresden, Department Of Neurology, Dresden, Germany, ³National Hospital for Neurology and Neurosurgery, Department Of Clinical And Movement Neurosciences, London, United Kingdom, ⁴BIAL-Portela & Ca S.A., Global Parkinson’s Disease Department, Coronado, Portugal

Background and Aims:: Opicapone (OPC) proved to be effective for end-of-dose motor fluctuations (MF) in Parkinson’s disease (PD) patients. The OPTIPARK study evaluated OPC 50mg in a heterogeneous population of patients treated in real-world conditions. We evaluated the influence of disease duration at baseline on the response to OPC in PD patients with MF.

Methods:: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. PD patients with MF received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy 3-month endpoint was Clinician’s-Global-Impression-of-Change (CGI-C). Secondary efficacy endpoints included Patient’s-Global-Impression-of-Change (PGI-C), 8-item PD-Questionnaire (PDQ-8), Unified-PD-Rating-Scale (UPDRS) and Non-Motor-Symptoms-Scale (NMSS). Safety assessments included evaluation of treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated the influence of disease duration at baseline in patients who completed the study for each outcome.

Results:: 393 (82.4%) patients completed the 3-month endpoint (completers-set, Table 1). Compared with patients with longer disease duration, a greater proportion of patients with shorter disease duration experienced ‘very much/much improvement’ on CGI-C and PGI-C (Table 2). Except for UPDRS, patients with shorter disease duration experienced greater improvements on quality of life (PDQ-8) and non-motor symptoms (NMSS), when compared to patients with longer disease duration (Table 3). Except for patients with PD duration ≥10.5 years, lower incidence of TEAEs considered at least possibly related to OPC were reported for patients with shorter disease duration (Table 3).

Table 1. Baseline characteristics (Completers-Set)

<table>
<thead>
<tr>
<th>Category</th>
<th>Age, mean (SD)</th>
<th>Male, n (%)</th>
<th>PD duration, mean (SD) years</th>
<th>Onset of MF, mean (SD) years</th>
<th>L-dopa amount, mean (SD) mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 6.5 years</td>
<td>≥ 6.5 years</td>
<td>&lt; 8.4 years*</td>
<td>≥ 8.4 years*</td>
<td>&lt; 10.5 years</td>
</tr>
<tr>
<td>N</td>
<td>179</td>
<td>214</td>
<td>204</td>
<td>189</td>
<td>293</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>65.8 (9.7)</td>
<td>68.1 (8.5)</td>
<td>66.1 (9.5)</td>
<td>68.5 (8.3)</td>
<td>66.7 (9.4)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>100 (55.9)</td>
<td>157 (73.4)</td>
<td>135 (66.2)</td>
<td>122 (64.6)</td>
<td>184 (62.8)</td>
</tr>
<tr>
<td>PD duration, mean (SD) years</td>
<td>4.2 (15)</td>
<td>11.3 (3.8)</td>
<td>5.0 (1.9)</td>
<td>12.5 (3.5)</td>
<td>6.0 (2.5)</td>
</tr>
<tr>
<td>Onset of MF, mean (SD) years</td>
<td>1.1 (1.1)</td>
<td>3.3 (3.5)</td>
<td>1.3 (1.6)</td>
<td>3.7 (3.7)</td>
<td>1.6 (1.8)</td>
</tr>
<tr>
<td>L-dopa amount, mean (SD) mg</td>
<td>506 (231)</td>
<td>595 (251)</td>
<td>524 (240)</td>
<td>599 (248)</td>
<td>536 (240)</td>
</tr>
</tbody>
</table>

*mean PD duration at baseline

L-dopa, levodopa; MF, motor fluctuations; PD, Parkinson’s disease SD; standard deviation
Conclusions:: These findings indicate that patients with shorter PD duration (representative of recent fluctuators) may have an added benefit from using OPC as adjunctive therapy to levodopa.
OPICAPONE ANALYSIS OF HEALTH ECONOMIC COSTS IN CLINICAL PRACTICE IN PARKINSON’S DISEASE UK PATIENTS WITH MOTOR FLUCTUATIONS: FINDINGS FROM THE OPTIPARK STUDY

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1National Hospital for Neurology and Neurosurgery, Department Of Clinical And Movement Neurosciences, London, United Kingdom, 2University of Dresden, Department Of Neurology, Dresden, Germany, 3BIAL-Portela & Ca S.A., Global Parkinson’s Disease Department, Coronado, Portugal

Background and Aims:: Opicapone (OPC) proved effective in treating end-of-dose motor fluctuations in Parkinson’s disease (PD) patients in two large trials. The OPTIPARK study evaluated OPC 50mg in a heterogeneous patient population treated in real-world conditions. Data from OPTIPARK were used to assess the influence of OPC treatment on the costs for the care of PD patients.

Methods:: OPTIPARK was a prospective, open-label, single-arm, multicentre trial conducted in Germany (3-month) and the UK (6-month). Patients with motor fluctuations received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy endpoint was Clinician’s Global Impression of Change after 3 months. Secondary endpoints included a health economic costs evaluation assessed by Client-Service-Receipt-Inventory (CSRI) questionnaire version adapted to assess the influence of the 6-month OPC treatment on the care costs of UK patients.

Results:: At baseline (N=128), total service costs during the previous 6 months were 284952.79 UK-£, mainly driven by primary/community care doctor (36.3%) and hospital doctor (18.8%) costs. At 6 months (N=95), total service costs were 121280.83 UK-£, mainly driven by hospital doctor (23.4%) and primary/community care doctor (23.2%) costs (Table 1). Average total costs at baseline were 13060 UK-£, including 2226 UK-£ for formal service and 11955 UK-£ for unpaid care costs. Average total costs decreased at 6 month by 3719 UK-£, including a reduction of 987 UK-£ for formal service and 2920 UK-£ for unpaid care costs (Table 2).

Table 1. Distribution of Service Costs by Visit – Full Analysis Set

<table>
<thead>
<tr>
<th></th>
<th>Baseline N = 128</th>
<th>6-month N = 95</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total service costs by visit (UK-£)</strong></td>
<td>284952.79</td>
<td>121280.83</td>
</tr>
<tr>
<td>Hospital doctor, n (%)</td>
<td>53546.36 (18.8)</td>
<td>28339.96 (23.4)</td>
</tr>
<tr>
<td>Day patient, n (%)</td>
<td>9680.7 (3.4)</td>
<td>1683.6 (1.4)</td>
</tr>
<tr>
<td>Residential care, n (%)</td>
<td>7289.28 (2.6)</td>
<td>2429.76 (2.0)</td>
</tr>
<tr>
<td>Inpatient, n (%)</td>
<td>20801.69 (7.3)</td>
<td>24242 (20.0)</td>
</tr>
<tr>
<td>General practitioner, n (%)</td>
<td>19430.4 (6.8)</td>
<td>7456.4 (6.1)</td>
</tr>
<tr>
<td>Primary/community care doctor, n (%)</td>
<td>103467.05 (36.3)</td>
<td>28103.75 (23.2)</td>
</tr>
<tr>
<td>Other health professional, n (%)</td>
<td>14332.57 (5.0)</td>
<td>8286.72 (6.8)</td>
</tr>
<tr>
<td>Social care, n (%)</td>
<td>25354.88 (8.9)</td>
<td>183.2 (0.2)</td>
</tr>
<tr>
<td>Investigations/tests, n (%)</td>
<td>4277.76 (1.5)</td>
<td>2787.79 (2.3)</td>
</tr>
<tr>
<td>Prostheses/adaptations, n (%)</td>
<td>26772.1 (9.4)</td>
<td>17767.65 (14.7)</td>
</tr>
</tbody>
</table>

a: costs of corresponding service category
Conclusions:: In PD patients with motor fluctuations treated in clinical practice in the UK, OPC 50mg had an apparent cost-saving impact.
LONG-TERM EFFICACY OF OPICAPONE IN THE REDUCTION OF ON-TIME WITH TROUBLESCOME DYSKINESIA IN PARKINSON’S DISEASE PATIENTS WITH MOTOR FLUCTUATIONS AND REPORTING TROUBLESCOME DYSKINESIA

Fabrizio Stocchi¹, Joaquim Ferreira², Olga Klepitskaya³, Diogo Magalhães⁴, José Rocha⁴, Patrício Soares-Da-Silva⁴

¹IRCCS San Raffaele Pisana, Department Of Neurology, Rome, Italy, ²Faculty of Medicine, University of Lisbon, Laboratory Of Clinical Pharmacology And Therapeutics, Lisbon, Portugal, ³Neurocrine Biosciences Inc., Neurology Department, San Diego, United States of America, ⁴BIAL-Portela & Ca S.A., Global Parkinson’s Disease Department, Coronado, Portugal

Background and Aims:: Opicapone (OPC) proved to be effective in treating end-of-dose motor fluctuations (MF) in Parkinson’s disease (PD) patients in two large multinational trials. We evaluated the evolution of ON-time with troublesome dyskinesia (‘Bad ON-time’) following OPC long-term exposure in PD patients with MF and reporting troublesome dyskinesia.

Methods:: Efficacy data from BIPARK-I and II were pooled for OPC 50mg. This post-hoc analysis evaluated the long-term effect of OPC on ‘Bad ON-time’ in patients randomized to OPC 50mg and already reporting troublesome dyskinesia at baseline, based on patient diaries.

Results:: Full Analysis Set included 216 patients. Of these, 44 (20.4%) patients reported ~2 h of ‘Bad ON-time’ and ~9 h of ON-time without or with non-troublesome dyskinesia (‘Good ON-time’) at baseline. Following initiation with OPC 50mg and up to the end of the double-blind period, an increase of ~1.4 h in ‘Good ON-time’ and decrease of ~5 mins in ‘Bad ON-time’ were observed, with an overall mean levodopa reduction of ~40 mg/day. By the end of the 1-year open-label extension (OLE) period, mean daily ‘Good ON-time’ had increased by approximately 2 h and mean daily ‘Bad ON-time’ had decreased by approximately 1 h. During the OLE, mean daily levodopa dose decreased by an additional 60 mg, ending in a total decrease of 100 mg.

Conclusions:: In PD patients with MF and reporting troublesome dyskinesia, OPC did not increase time with troublesome dyskinesia; in fact, OPC long-term exposure, associated with levodopa dose reduction, led to a relevant reduction of ‘Bad ON-time’ and increase of ‘Good ON-time’.
HIGH RESOLUTION ULTRASOUND SHOWS AXONAL DEGENERATION OF THE VAGUS NERVE IN IDIOPATHIC PARKINSON’S DISEASE

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Background and Aims:: Previous histopathological studies revealed degeneration of the dorsal motor nucleus of the Vagus Nerve (VN) early in Idiopathic Parkinson’s Disease (IPD). Degeneration of VN axons should be detectable by High –Resolution Ultrasound (HRUS) as a thinning of the nerve trunk. In order to establish if the VN exhibits sonographic signs of atrophy in IPD, we investigated patients with IPD compared with age-matched controls.

Methods:: We measured the caliber (cross-sectional area, CSA) and perimeter of the VN in 20 pt. with IPD (8 females and 12 males; mean age 73.0 + 8.6 yrs) and in age-matched controls using HRUS. Evaluation were performed by blinded raters using an Esaote MyLabGamma device in conventional B-Mode with an 8-19 MHz probe.

Results:: In both sides, the VN-CSA was significant smaller in IPD pt. than in controls (right 2,37 + 0.91, left 1.87 + 1.35 mm² versus 6.0 + 1.33, 5.6 + 1.26 mm²;p <0.001), as well as the perimeter (right 5.06 + 0.85, left 4.78 + 1.74 mm versus 8.87 + 0.86, 8.58 + 0.97 mm; p <0.001). There was no significant correlations between VN-CSA and age, the Hohen & Yahr scale, L-dopa therapy and disease duration.

Conclusions:: Our data provide evidence of atrophy of the VNs in IPD patients by HRUS. Moreover, HRUS of the VN represent a non-invasive easy imaging modality of screening in IPD patients independent of disease stage and duration, and an interesting possible additional index of disease.
EFFECT OF TIANEPTINE ON DEPRESSION IN PARKINSON’S DISEASE, AN OBSERVATIONAL PILOT STUDY

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Background and Aims:: Depression is frequent in Parkinson’s disease (PD). Glutamate is a neurotransmitter involved in non-dopaminergic dysfunction in PD and could be associated with depression. In this sense, tianeptine, an antidepressant with an atypical mechanism of action modulating glutamate, could be useful to treat depression in PD. The aim of this study was to assess the antidepressant effect and safety of tianeptine in PD.

Methods:: We retrospectively analyzed the 17-item Hamilton depression rating scale (HAMD-17) in PD patients treated with tianeptine at the end of follow-up compared to baseline. Comparisons were conducted using the Wilcoxon test (p<0.05). Criteria for total response, partial response and non-response were defined as ≥50%, 25%–49% and <25% of improvement. For depression severity the criteria were: remission (HAMD-17 ≤7), mild (HAMD-17=8-16), moderate (HAMD-17=17-23) and severe (HAMD-17 ≥24). Adverse events were also assessed. Data were shown as median[range]

Results:: n=11, female=8/11, age(years)=77[62-95], Hoehn&Yahr=3[1-4], levodopa equivalent dose(mg/day)=400[200-950], follow-up(months)=4[1-6]. Baseline data: HAMD-17=19[8-24], depression severity: mild=2/11 moderate=8/11 severe=1/11. Data at the end of follow-up: HAMD-17=17[6-22], HAMD-17 improvement=4[0-7], p=0.0073, average improvement of 21% (no patient showed total response but 5/11 showed partial response), depression severity: remission 2/11 mild 3/11 moderate 6/11 (6/11 improved depression severity). 1/11 patients showed mild adverse events (discomfort and dizziness)

Conclusions:: We reported a moderate and significant improvement of depression in PD patients treated with tianeptine with two patients showing remission. It supports the role of glutamate in depression development in PD. Tianeptine was well tolerated. Further studies are needed to confirm our findings and to establish factors of better response.
Efficacy of Opicapone at Different Levodopa Regimens Up to a Threshold of 600 mg/day Levodopa in Parkinson’s Disease Patients with Motor Fluctuations

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Background and Aims:: Opicapone (OPC) proved to be effective for end-of-dose motor fluctuations in Parkinson’s disease (PD) patients. We evaluated the efficacy of OPC in PD patients with motor fluctuations being treated with different levodopa regimens up to a threshold of 600 mg/day levodopa.

Methods:: Efficacy data from BIPARK-I and II were combined for the placebo (PLC) and OPC-50mg groups. Primary efficacy endpoint was change from baseline in OFF-time. Subgroup analyses were performed to evaluate the efficacy of OPC-50mg in different levodopa regimens up to a threshold of 600 mg/day levodopa (300–400, 400–500 and 500–600 mg/day).

Results:: Full Analysis Set included 239 patients (PLC, n=118; OPC-50mg, n=121). Mean OFF-time reduction was at least two-fold greater than PLC when OPC-50mg was added to any levodopa regimen: mean (95% confidence interval) changes from baseline in absolute OFF-time for OPC-50mg versus PLC were -102.2 (-138.1, -66.3) versus -53.4 (-89.6, -17.3) min for patients treated with levodopa 300–400 mg/day, -110.0 (-146.7, -73.3) versus -37.2 (-77.7, 3.3) min for patients treated with levodopa 400–500 mg/day, and -117.6 (-152.6, -82.6) versus -23.1 (-67.8, 21.6) min for patients treated with levodopa 500–600 mg/day. It was notable that, with increasing levodopa dose regimens, there was a trend towards decreasing magnitude of effect in the PLC group, compared with a trend towards a slight increase in magnitude of effect in the OPC-50mg group (Figure 1).
Conclusions:: OPC-50mg showed at least a two-fold greater OFF-time reduction than placebo, with a slight increase in magnitude of effect with increasing levodopa regimens.
EFFICACY OF OPICAPONE ACCORDING TO DIFFERENT LEVODOPA DAILY INTAKES IN PARKINSON’S DISEASE PATIENTS WITH MOTOR FLUCTUATIONS

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Background and Aims:: Opicapone (OPC), a once-daily catechol-O-methyltransferase inhibitor, proved to be effective in treating end-of-dose motor fluctuations in Parkinson’s disease (PD) patients in two large multinational trials. We evaluated the efficacy of OPC in PD patients with motor fluctuations according to different levodopa daily intakes.

Methods:: Efficacy data from BIPARK-I and II were combined for the placebo (PLC) and OPC 50 mg groups. The studies had similar designs, eligibility criteria and methodologies. Primary efficacy endpoint was change from baseline in absolute OFF-time. Safety was assessed by evaluating the incidence of treatment-emergent adverse events (TEAEs). Subgroup analyses were performed to evaluate consistency and potential trends between subgroups based on different levodopa daily intakes at baseline (Table 1). Efficacy pairwise subgroup analyses were performed using Analysis of Covariance. Safety assessments were analysed descriptively.

Results:: Overall, 522 patients were randomised to PLC (n=257) and OPC 50 mg (n=265) (Table 1). OPC 50 mg was significantly more effective than PLC for all subgroup analyses (p<0.05), except for the subgroup of patients treated with ≥6 levodopa daily intakes (p=0.0623; Table 2). Moreover, OPC 50 mg demonstrated enhanced magnitude of effect in patients who had less frequent levodopa intakes (Table 2). There was also a trend towards a lower incidence of dopaminergic-related TEAEs in the same subgroups of patients (Table 3).

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Table 1. Baseline characteristics of OPC 50 mg patient subgroups (Safety Set)

<table>
<thead>
<tr>
<th>L-dopa intakes (n)</th>
<th>Age, years</th>
<th>PD duration, years</th>
<th>OFF-time, h</th>
<th>Onset of MF, years</th>
<th>H&amp;Y(at ON)</th>
<th>Male gender</th>
<th>L-dopa, mg</th>
<th>L-dopa use, years</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;4</td>
<td>60</td>
<td>65.5 (9.4)</td>
<td>5.6 (2.6)</td>
<td>6.0 (1.7)</td>
<td>1.7 (1.6)</td>
<td>2.3 (1.6)</td>
<td>40 (50)</td>
<td>485.8 (198.4)</td>
</tr>
<tr>
<td>≥2</td>
<td>205</td>
<td>64.8 (8.7)</td>
<td>8.2 (4.5)</td>
<td>6.3 (2.1)</td>
<td>3.1 (3.1)</td>
<td>2.5 (1.5)</td>
<td>30 (50)</td>
<td>759.8 (135.8)</td>
</tr>
<tr>
<td>&lt;5</td>
<td>132</td>
<td>65.4 (9.1)</td>
<td>6.0 (3.0)</td>
<td>6.0 (1.9)</td>
<td>2.0 (1.9)</td>
<td>2.4 (1.6)</td>
<td>84 (63.8)</td>
<td>560.4 (250.8)</td>
</tr>
<tr>
<td>≥2</td>
<td>25</td>
<td>63.6 (8.5)</td>
<td>9.3 (4.7)</td>
<td>6.5 (2.2)</td>
<td>3.6 (3.5)</td>
<td>2.4 (1.5)</td>
<td>76 (15.1)</td>
<td>835.3 (277.4)</td>
</tr>
<tr>
<td>≥6</td>
<td>60</td>
<td>64.6 (9.1)</td>
<td>6.9 (3.8)</td>
<td>6.1 (2.0)</td>
<td>2.4 (2.7)</td>
<td>2.4 (2.5)</td>
<td>127 (92.0)</td>
<td>634.4 (286.3)</td>
</tr>
<tr>
<td>≥6</td>
<td>60</td>
<td>64.2 (9.0)</td>
<td>10.1 (4.9)</td>
<td>6.9 (2.2)</td>
<td>3.9 (3.3)</td>
<td>3.5 (3.5)</td>
<td>197 (9.5)</td>
<td>917.1 (346.1)</td>
</tr>
</tbody>
</table>

Rows shaded in grey indicate variables generally associated with earlier disease course: i.e. lower L-dopa intakes, in comparison with matched unshaded rows
H&Y, H&Y: SMD and ratio; L-dopa, levodopa; MF, motor fluctuations; PLC, placebo; PD, Parkinson’s disease; SD, standard deviation.

Table 2. Efficacy of OPC 50 mg and difference versus PLC in specific subgroup analyses (IAS)

<table>
<thead>
<tr>
<th>L-dopa intakes (n)</th>
<th>Δ vs PLC (SE)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥4</td>
<td>-124.5 (20.1)</td>
<td>0.0397</td>
</tr>
<tr>
<td>≥2</td>
<td>-114.1 (11.1)</td>
<td>0.0161</td>
</tr>
<tr>
<td>≥5</td>
<td>-118.2 (13.7)</td>
<td>0.0024</td>
</tr>
<tr>
<td>≥2</td>
<td>-114.7 (17.7)</td>
<td>0.0016</td>
</tr>
<tr>
<td>≥6</td>
<td>-120.6 (11.3)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Rows shaded in grey indicate variables generally associated with earlier disease course: i.e. lower L-dopa intakes, in comparison with matched unshaded rows. Values shown in bold indicate variables for which the difference in change from baseline in OFF-time for OPC 50 mg versus PLC (≥4 vs PLC) was greater than that of the matched comparative row FAS, Full Analysis Set; H&Y, H&Y: SMD and ratio; L-dopa, levodopa; IAS, least square; OPC, opicapone; PD, Parkinson’s disease; PLC, placebo; SE, standard error.
Conclusions:: These findings indicate that OPC 50 mg is efficacious in the full spectrum of motor fluctuations and could be considered earlier in PD patients.

<table>
<thead>
<tr>
<th>L-dopa intakes (n)</th>
<th>N</th>
<th>Any TEAE, n (%)</th>
<th>Any related TEAE, n (%)</th>
<th>Incidence of related TEAEs (dopaminergic-related), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dykinesia</td>
</tr>
<tr>
<td>&lt;4</td>
<td>60</td>
<td>30 (50%)</td>
<td>15 (25%)</td>
<td>4 (7%)</td>
</tr>
<tr>
<td>≥4</td>
<td>209</td>
<td>140 (68%)</td>
<td>98 (48%)</td>
<td>56 (24%)</td>
</tr>
<tr>
<td>≥5</td>
<td>115</td>
<td>97 (73%)</td>
<td>77 (64%)</td>
<td>41 (31%)</td>
</tr>
<tr>
<td>&lt;8</td>
<td>205</td>
<td>126 (62%)</td>
<td>75 (37%)</td>
<td>32 (15%)</td>
</tr>
<tr>
<td>≥8</td>
<td>60</td>
<td>44 (73%)</td>
<td>38 (63%)</td>
<td>21 (38%)</td>
</tr>
</tbody>
</table>

Rows shaded in grey indicate variables generally associated with earlier disease course (i.e. lower L-dopa intake), in comparison with matched unshaded rows.

L-dopa, levodopa, OPC, opicapone; TEAE, treatment-emergent adverse event (preferred term shown for dopaminergic TEAEs).
IMPACT OF 3-MONTH EARLIER VERSUS LATER INITIATION OF OPICAPONE VERSUS ENTACAPONE IN LEVODOPA-TREATED PATIENTS WITH PARKINSON'S DISEASE AND MOTOR FLUCTUATIONS

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Background and Aims:: Opicapone (OPC) proved to be effective for end-of-dose motor fluctuations in Parkinson’s disease (PD) patients.  
Methods:: OPC 50 mg and entacapone (ENT) data from the BIPARK-I study were analyzed. The primary efficacy endpoint was change from baseline in absolute OFF-time. Secondary endpoints included ON-time without dyskinesia, Unified-PD-Rating-Scale (UPDRS)-II and III. Patients receiving levodopa/dopa-decarboxylase inhibitor (DDCi) were randomized to OPC 50 mg or ENT for a 3-month, double-blind phase, after which all patients received open-label levodopa/DDCi plus OPC for up to 1 year. This post-hoc analysis evaluated the impact of 3-month earlier versus later initiation of OPC by comparing outcomes of patients who received OPC in the double-blind phase (‘early start’) with those who received ENT in the double-blind phase and then switched to OPC (‘later start’), at the end of the double-blind phase and at a 3-month cut-off after the initiation of the open-label phase.  
Results:: Overall, 198 patients switched from OPC 50 mg (n=98) or ENT (n=100) to 1-year OPC open-label extension (Table 1). At the 3-month double-blind endpoint, OPC versus ENT showed a greater reduction in OFF-time, UPDRS-II and III, and an increase in ON-time without dyskinesia (Table 2; Figure 1). At the 3-month open-label cut-off, OPC ‘early start’ versus ‘later start’ showed a greater reduction in OFF-time, UPDRS-III, and an increase in ON-time without dyskinesia (Table 2; Figure 1). OPC 50 mg was well tolerated by both groups.

Table 1. Baseline characteristics (Safety set)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DB ENT/OL OPC N=100</th>
<th>DB OPC 50 mg/OL OPC N=98</th>
</tr>
</thead>
<tbody>
<tr>
<td>At double-blind baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>64 (64.0)</td>
<td>61 (62.2)</td>
</tr>
<tr>
<td>Age, mean years</td>
<td>63.2</td>
<td>63.3</td>
</tr>
<tr>
<td>Disease duration, mean years</td>
<td>7.6</td>
<td>7.4</td>
</tr>
<tr>
<td>Daily OFF-time, mean hours</td>
<td>6.4</td>
<td>6.2</td>
</tr>
<tr>
<td>At open-label baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily OFF-time, mean hours</td>
<td>4.9</td>
<td>4.3</td>
</tr>
<tr>
<td>Presence of dyskinesia† – yes, n (%)</td>
<td>43 (43.0)</td>
<td>41 (41.8)</td>
</tr>
<tr>
<td>Daily levodopa dose, mean mg</td>
<td>606.0</td>
<td>675.2</td>
</tr>
</tbody>
</table>

†From Unified Parkinson’s Disease Rating Scale IV item-32
DB, double-blind; ENT, entacapone; OL, open-label; OPC, opicapone
Conclusions:
These data suggest that early rather than later initiation of OPC to levodopa/DDCi provides an extended benefit over ENT.
INSUFFICIENT TREATMENTS OF PATIENTS WITH PARKINSON’S DISEASE RECEIVING HOME MEDICAL CARES AND IN NURSING HOMES

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Trinity Neurology Clinic, Neurology, Sakura City, Chiba, Japan

Background and Aims:: Patients with Parkinson’s disease (PD) may be destined to receive home medical cares (HMCs) or enter nursing homes (NHs) because PD is a progressive disease. I am worried about stopped consultation with neurologists and treated insufficiently after receiving HMCs or entering NHs on patients with PD. So, I planned to investigate consultation with neurologists and treatments about patients with PD receiving HMCs and entering NHs.

Methods:: I send questionnaires with faxes to all visiting doctor offices, all visiting nurse stations, and all nursing homes in Sakura city. I asked with these questionnaires whether they had patients with PD or not, and whether the patients continuously consulted neurologist or not. I also asked with these questionnaires the patient’s ages, sexes, ages at onsets, disease durations, Hoehn & Yahr (HY) stages and medications.

Results:: Twenty-one (35%) of sixty facilities answered to my questionnaires with total forty-five patients with PD. Twenty-nine of these patients with PD continuously consulted neurologists and sixteen did not. Male sexes in the patients consulting neurologists or not were 12 (41.4%) and 6 (37.5%), average ages were 77.9±7.4 and 80.7±6.5, average ages at onsets were 69.3±10.8 and 69.3±7.7 years old, disease durations were 8.6±6.9 and 10.3±5.5 years, HY stages were 3.7±1.2 and 4.3±1.1, and levodopa equivalent daily doses were 416±295 and 309±263 mg/day, respectively.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Sex</th>
<th>Age (Years)</th>
<th>Disease Onset (Years)</th>
<th>Disease Duration (Years)</th>
<th>HY Stage</th>
<th>LDEE (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td></td>
<td>78.9</td>
<td></td>
<td></td>
<td>3.9</td>
<td>377</td>
</tr>
<tr>
<td>Neurologists (+)</td>
<td></td>
<td>77.9</td>
<td></td>
<td></td>
<td>3.7</td>
<td>416</td>
</tr>
<tr>
<td>Neurologists (-)</td>
<td></td>
<td>80.7</td>
<td></td>
<td></td>
<td>4.3</td>
<td>309</td>
</tr>
</tbody>
</table>
Conclusions:: Within the patients with PD receiving HMCs and in NHs, the patients not continuously consulting neurologists were older, received less medication and had more motor severities than the patients continuously consulting neurologists.
Background and Aims: Cannabis use is frequent in Parkinson disease (PD), despite limited data regarding effects. This study aims to determine efficacy and tolerability of relatively high cannabidiol (CBD) and low D-9-tetrahydrocannabinol (THC) in 60 persons with PD. Interim data on tolerability is presented.

Methods: In this randomized, double-blind, controlled, parallel study participants that took a CBD cannabis extract (from National Institute of Drug Abuse) oral sesame oil solution with 100mg/mL CBD and 3.33mg/mL THC. Study drug started at 1.25mg/kg/day and increased to 2.5mg/kg/day CBD for 10-14 days. Unblinded study staff assigned participants to two groups, A or B, according to treatment randomization, which were matched in age, sex and stage of disease.

Results: Between 09/2018 and 04/2020, 41 (66% men) took study drug: mean age 69.2 (SD 7.4). Mean daily dose was 2.3 (0.4) mg/kg/day, i.e., 189.6 (55.3) mg CBD and 6.3 (1.8) mg THC, and participants were on study drug for 16.5 (5.6) days. Group A (n=22) reported AEs 206 times (2 SAEs), and 19 (86%) reported an AE: dizziness (59%); fatigue, feeling of relaxation, headache, decreased concentration, (36%); feeling abnormal, feeling drunk, nausea, somnolence (27%); confusion, (23%). Group B (n=19) reported AEs 93 times (no SAEs), and 17 (89%) reported an AE: headache (37%); somnolence (26%); feeling of relaxation (21%). Most AEs were mild; one participant withdrew due to intolerance.

Conclusions: Interim data suggests relatively high CBD/low THC (likely Group A) is well tolerated in PD, with a broad range of mild AEs.
EP0677 / #1230

EFFICACY OF OPICAPONE ACCORDING TO LEVODOPA’S DURATION OF USE IN PARKINSON’S DISEASE PATIENTS WITH MOTOR FLUCTUATIONS

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Background and Aims:: Opicapone (OPC), a once-daily catechol-O-methyltransferase inhibitor, proved to be effective in treating end-of-dose motor fluctuations in Parkinson’s disease (PD) patients in two large multinational trials. We evaluated the efficacy of OPC in PD patients with motor fluctuation according to levodopa’s duration of use.

Methods:: Efficacy data from BIPARK-I and II were combined for the placebo (PLC) and OPC 50 mg groups. The studies had similar designs, eligibility criteria and methodologies. Primary efficacy endpoint was change from baseline in absolute OFF-time. Safety was assessed by evaluating the incidence of treatment-emergent adverse events (TEAEs). Subgroup analyses were performed to evaluate consistency and potential trends between subgroups based on levodopa’s duration of use at baseline (Table 1). Efficacy subgroup analyses were performed using Analysis of Covariance. Safety assessments were analysed descriptively.

Results:: Overall, 522 patients were randomised to PLC (n=257) and OPC 50 mg (n=265) (Table 1). OPC 50 mg was significantly more effective than PLC for all subgroup analyses (p<0.05), except for the subgroup of patients treated with levodopa for ≥7 years and ≥8 years (Table 2). Moreover, OPC 50 mg demonstrated enhanced efficacy in patients with shorter levodopa treatment duration in each subgroup threshold (Table 2). There was also a trend towards a lower incidence of dopaminergic-related TEAEs in the same subgroups of patients (Table 3).
Conclusions: These findings indicate that there may be an added benefit from using OPC 50 mg earlier in a course of treatment with levodopa and promptly in the motor fluctuations spectrum of PD.
OPICAPONE IN CLINICAL PRACTICE IN PARKINSON’S DISEASE PATIENTS WITH MOTOR FLUCTUATIONS AND COMPLICATIONS OF THERAPY AT BASELINE: FINDINGS FROM THE OPTIPARK STUDY

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Background and Aims:: Opicapone (OPC) proved to be effective for end-of-dose motor fluctuations (MF) in Parkinson’s disease (PD) patients. The OPTIPARK study evaluated OPC 50mg in a heterogeneous population of patients treated in real-world conditions. We evaluated OPC’s effects in patients with MF and complications of therapy (CoT) at baseline.

Methods:: OPTIPARK was a prospective, open-label, single-arm trial conducted in Germany and the UK. Patients with MF received OPC 50mg in addition to current antiparkinsonian treatment. Primary efficacy 3-month endpoint was Clinician’s-Global-Impression-of-Change. Secondary assessments included Unified-Parkinson’s-Disease-Rating-Scale (UPDRS) and treatment-emergent adverse events (TEAEs). This post-hoc analysis evaluated OPC’s impact in patients who completed the study and reported CoT at baseline, assessed by UPDRS IV.A-32 (waking-day-dyskinesias [WdD]).

Results:: 393 (82.4%) patients completed the 3-month endpoint (completers-set); 150 reported WdD at baseline (Table 1). Most baseline WdD were not -or mildly- disabling and not -or slightly- painful. Approximately 26% of WdD completers reported dyskinesia as TEAE. At endpoint, most of the patients (131 [88%]) demonstrated either maintained (54%) or improved (34%) WdD. Most remaining WdD were still not -or mildly- disabling and also not -or slightly- painful (Table 2, Figure 1). Notably, none worsened to either severe -or complete- disabling and severe -or marked- painful. Approximately 54% of dyskinesias reported as TEAE resolved following a mean daily levodopa decrease of ~67 mg (Table 2).

<table>
<thead>
<tr>
<th>Table 1. Demographics and other baseline characteristics (completers set)</th>
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<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
</tr>
<tr>
<td>Age, mean (SD) years</td>
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<tr>
<td>L-dopa amount (mg), mean (SD)</td>
</tr>
<tr>
<td>Disease duration, mean (SD) years</td>
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<tr>
<td>Duration of motor fluctuations, mean (SD) years</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>UPDRS IV. Complications of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Dyskinesias</td>
</tr>
<tr>
<td>32. What proportion of the waking day are dyskinesias present?</td>
</tr>
<tr>
<td>None, n (%)</td>
</tr>
<tr>
<td>L-dopa amount (mg), mean (SD)</td>
</tr>
<tr>
<td>1–25% of day, n (%)</td>
</tr>
<tr>
<td>26–50% of day, n (%)</td>
</tr>
<tr>
<td>51–75% of day, n (%)</td>
</tr>
<tr>
<td>76–100% of day, n (%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Baseline (N=393)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-dopa (mg), mean (SD)</td>
</tr>
</tbody>
</table>

SD, standard deviation
Table 2. Follow-up of patients that reported dyskinesia during waking day at baseline

<table>
<thead>
<tr>
<th>UPDRS IV. Complications of Therapy</th>
<th>Baseline (N=149+)</th>
<th>During the study</th>
<th>Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Dyskinesias</td>
<td></td>
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<tr>
<td>32. What proportion of the waking</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>day are dyskinesias present?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None, n (%)</td>
<td>96 (64.4)</td>
<td>66 (44.3)</td>
<td>89 (59.7)</td>
</tr>
<tr>
<td>1–25% of day, n (%)</td>
<td>18 (12.1)</td>
<td>12 (8.1)</td>
<td>22 (14.8)</td>
</tr>
<tr>
<td>26–50% of day, n (%)</td>
<td>38 (25.5)</td>
<td>10 (6.7)</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>51–75% of day, n (%)</td>
<td>10 (6.7)</td>
<td>2 (1.3)</td>
<td>8 (5.4)</td>
</tr>
<tr>
<td>76–100% of day, n (%)</td>
<td>5 (3.4)</td>
<td>0</td>
<td>6 (4.0)</td>
</tr>
<tr>
<td>33. How disabling are the</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dyskinesias?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not disabling, n (%)</td>
<td>64 (43.0)</td>
<td>54 (36.2)</td>
<td>80 (53.7)</td>
</tr>
<tr>
<td>Mildly disabling, n (%)</td>
<td>44 (29.5)</td>
<td>23 (15.4)</td>
<td>50 (33.6)</td>
</tr>
<tr>
<td>Moderately disabling, n (%)</td>
<td>34 (22.8)</td>
<td>8 (5.4)</td>
<td>18 (12.1)</td>
</tr>
<tr>
<td>Severely disabling, n (%)</td>
<td>7 (4.7)</td>
<td>1 (0.7)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Completely disabled, n (%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>34. How painful are the</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dyskinesias?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No painful dyskinesias, n (%)</td>
<td>111 (74.5)</td>
<td>101 (67.8)</td>
<td>117 (78.5)</td>
</tr>
<tr>
<td>Slight, n (%)</td>
<td>21 (14.1)</td>
<td>8 (5.4)</td>
<td>21 (14.1)</td>
</tr>
<tr>
<td>Moderate, n (%)</td>
<td>15 (10.1)</td>
<td>5 (3.4)</td>
<td>10 (6.7)</td>
</tr>
<tr>
<td>Severe, n (%)</td>
<td>1 (0.7)</td>
<td>0</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Marked, n (%)</td>
<td>1 (0.7)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Reported Dyskinesias as</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TEAE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any dyskinesia, n (%)</td>
<td>-</td>
<td>39 (26.2)</td>
<td>18 (12.1)</td>
</tr>
<tr>
<td>L-dopa amount (mg), mean (SD)</td>
<td>644.9 (237)</td>
<td>-</td>
<td>577.6 (272)</td>
</tr>
<tr>
<td>Mild</td>
<td>-</td>
<td>31 (79.5)</td>
<td>14 (77.8)</td>
</tr>
<tr>
<td>Moderate</td>
<td>-</td>
<td>9 (23.1)</td>
<td>4 (22.2)</td>
</tr>
<tr>
<td>Related†</td>
<td>-</td>
<td>32 (82.1)</td>
<td>13 (72.2)</td>
</tr>
<tr>
<td>Unlikely/unrelated</td>
<td>-</td>
<td>85 (20.5)</td>
<td>5 (27.8)</td>
</tr>
</tbody>
</table>

* One subject had missing data at endpoint; † related TEAEs are defined as being at least possible related; § one subject reported both mild and moderate; $$ one subject reported both unlikely and probable; Imp., improved; Maint., maintained; TEAE, treatment emergent adverse event; Wors., worsened adverse event.


**Conclusions:**

OPC was not associated with a clear WdD worsening in patients already reporting CoT; more than double of the patients reported WdD improvement rather than worsening.

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**Figure 1.** Follow-up of patients that reported dyskinesia during waking day at baseline
DRIVING MOTOR CORTEX OSCILLATIONS MODULATES BRADYKINESIA IN PARKINSON’S DISEASE

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Sapienza University of Rome, Department Of Human Neurosciences, Rome, Italy

**Background and Aims::** In Parkinson’s disease (PD), beta (β) and gamma (γ) oscillations are altered in the basal ganglia, and this abnormality contributes to bradykinesia pathophysiology. However, it is unclear whether β and γ rhythms at the primary motor cortex (M1) level influence bradykinesia. We aimed at clarifying this issue by using transcranial alternating current stimulation (tACS), a neurophysiological technique that enhances cortical rhythms by entraining endogenous oscillations.

**Methods::** We tested whether β- and γ-tACS on M1 modulate bradykinesia in PD patients by analyzing the kinematic features of repetitive finger tapping. We also verified whether possible tACS-induced bradykinesia changes depended on modifications in specific M1 circuits, as assessed by short-interval intracortical inhibition (SICI) and short-latency afferent inhibition (SAI). Patients were studied OFF and ON therapy.

**Results::** Movement velocity significantly worsened during β-tACS and movement amplitude improved during γ-tACS, while the sequence effect did not change. In addition, SAI decreased (reduced inhibition) during β-tACS and SICI decreased during both γ- and β-tACS. The effects of tACS were comparable between OFF and ON sessions. In patients OFF therapy, the degree of SICI modulation during β- and γ-tACS correlated with movement velocity and amplitude changes, respectively. Moreover, there was a positive correlation between the effect of γ-tACS on movement amplitude and motor symptoms severity.

**Conclusions::** Our results demonstrate that β and γ oscillations at the M1 level are relevant in the pathophysiology of bradykinesia in PD. Changes in inhibitory GABA-A-ergic interneuronal activity may reflect compensatory M1 mechanisms to counteract bradykinesia.
LONG-TERM EFFECT OF SAFINAMIDE ON PRIMARY MOTOR CORTEX EXCITABILITY AND PLASTICITY IN PARKINSON’S DISEASE: A TMS STUDY

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¹Sapienza University of Rome, Department Of Human Neurosciences, Rome, Italy, ²IRCCS Neuromed, Irccs Neuromed, Pozzilli, Italy

Background and Aims:: In a recent Transcranial Magnetic Stimulation (TMS) study, we demonstrated abnormally enhanced Short-Interval Intracortical Facilitation (SICF) in patients with Parkinson’s Disease (PD). These abnormalities reflect increased glutamatergic transmission in primary motor cortex (M1). A short-term treatment with safinamide at 100 mg/day can restore SICF in PD by reducing glutamatergic transmission via blockade of voltage-gated sodium channels. We here examined the long-term effect of chronic treatment with safinamide 100 mg/day on SICF and other measures of M1 excitability and plasticity in PD.

Methods:: 25 PD patients underwent 3 separate sessions: before starting safinamide (T0), after 2 weeks (T1) and after 12 months (T2) of safinamide 100 mg/day. Patients were tested when OFF and ON therapy. Motor evaluation included MDS-UPDRS-II and UDysRS-III. We tested Input/output curve, Short-Interval Intracortical Inhibition (SICI), Intracortical Facilitation (ICF) and SICF. In a subgroup of 15 patients, we also examined responses to intermittent theta burst stimulation (iTBS).

Results:: UPDRS-III and UDysRS-III scores were comparable at T0-T1-T2, indicating overall clinical stability over one-year follow-up. In PD patients, safinamide 100 mg/day restored SICF at both T1 and T2. Moreover, safinamide improved responses to iTBS at T1 and T2. Drug-induced changes in SICF correlated with responses to iTBS at T2.

Conclusions:: Our results overall support the pathophysiological role of abnormally enhanced glutamatergic transmission in M1 in PD patients. Safinamide at 100 mg/day induces short- and long-term improvement of excitability and plasticity measures in M1. These results support the antigu glutamatergic effect of the drug when given at 100 mg/day.
THE ANTIPARKINSONIAN DRUG SAFINAMIDE IS NOT HARMFUL FOR THE HUMAN RETINA. A NEUROPHYSIOLOGICAL STUDY

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¹ASL 3 Genovese, Neurology, Genova, Italy, ²ASL 2 Savonese, Neurology, Savona, Italy, ³IRCCS Policlinico Ospedale San Martino, Di. N.o.g.mi, Genova, Italy

Background and Aims:: Safinamide is a selective MAO-B inhibitor, indicated for the treatment of Parkinson's disease (PD). The European patient information leaflet warns about the "Potential for retinal degeneration in patients with presence/prior history of retinal disease: Safinamide should not be administered to patients with ophthalmological history that would put them at increased risk for potential retinal effects". The available literature, however, misses any data concerning this potential retinal toxicity. This prompted us to implement a neurophysiological study concerning a possible drug-related retinal damage.

Methods:: Twenty PD patients were investigated. All patients had corrected visual acuity above 7/10. Safinamide was titrated to 100 mg/day over 15 days. All the subjects underwent a neurophysiological study of the visual function, namely full field ERG, multifocal ERG (mfERG), pattern ERG (PERG) and pattern VEP. The neurophysiological and clinical (UPDRS) evaluations were carried out at the same time of the day, at the baseline, after one, six and twelve months.

Results:: PD patients showed a significant delay of the latency values of PERG and VEP, while ERG and mfERG results were within the normal limits. Over one year, however, ERG, mfERG, PERG and PEV did not show any significant changes. No visual disturbances were reported. The mean UPDR scores improved significantly (p <0.01).

Conclusions:: The current results provide evidence that Safinamide is not harmful for the human retina, both for diffuse (full field ERG) and focal (mfERG, PERG) functional damage, even over a long period of time (one year). The optic nerve (VEP) was not involved as well.
COMBINED GCASE/ALPHA-SYNUCLEIN PATTERN MAY IDENTIFY SPECIFIC PRODOMAL PD PATTERNS IN GBA CARRIERS: A CLUSTER ANALYSIS STUDY

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¹Department of Brain and Behavioural Sciences, University of Pavia, Neurorehabilitation Unit, Ircs Mondino Foundation, PAVIA, Italy, ²IRCCS Mondino Foundation, Cellular And Molecular Neurobiology Unit, Pavia, Italy, ³University Institute for Advanced Studies, Human and Life Sciences, Irccs Mondino Foundation, Cognitive Computational Neuroscience Research Unit, Pavia, Italy, ⁴Department of Brain and Behavioural Sciences, University of Pavia, Cognitive Computational Neuroscience Research Unit, Ircs Mondino Foundation, Pavia, Italy, ⁵UCL Queen Square Institute of Neurology, Department Of Clinical And Movement Neurosciences, London, United Kingdom, ⁶Royal Free Hospital and Department of Haematology, UCL, Lysosomal Storage Disorders Unit, London, United Kingdom, ⁷Department of Molecular Medicine, University of Pavia, Neurogenetics Research Centre, Ircs Mondino Foundation, Pavia, Italy, ⁸Department of Brain and Behavioural Sciences, University of Pavia, Cellular And Molecular Neurobiology Unit, Ircs Mondino Foundation, Pavia, Italy

Background and Aims:: Glucocerebrosidase (GBA) gene mutations are the most frequent genetic risk factor for Parkinson Disease (PD). Relationship between GBA status and increased risk for GBA-PD is still unclear. We investigated whether glucocerebrosidase activity (GCase) and α-synuclein levels in blood cells in asymptomatic subjects carrying GBA mutations (GBA carriers) are associated with a more severe prodromal PD profile.

Methods:: 31 GBA carriers, 28 GBA-PD and 38 healthy controls (HC) were enrolled in this study. A two-step cluster analysis was performed to split the subjects into different clusters based on their biochemical profile analysing GCase and α-synuclein separately and in combination. Motor and non-motor features (UPDRS-III, BDI, SCOPA-AUT, MoCA, RBDsq, PDSS, UPSIT) for prodromal PD were merged in a 7-item cumulative clinical index (CI). One-way ANOVA assessed the effect of cluster analysis groupings on the CI.

Results:: Cluster analysis based on combined GCase activity/α-synuclein levels provided the best performance splitting the sample into a benign (high GCase/mid-low α-synuclein) and malignant (low GCase/high α-synuclein) profile, discriminating HC from both GBA carriers and GBA-PD. Therefore we found a significant effect of combined GCase/α-synuclein clusters (F(1.95)=15.495, p<0.001) on clinical profile, revealing a significant difference between the malignant and the benign profiles, with the first showing significantly higher values in the CI with dysautonomia, mood and sleep disorders as the most relevant features.

Conclusions:: Our study provides novel information about the relationship between biochemical and phenotypic prodromal PD signatures of GBA carriers.
LONGITUDINAL CLINICAL, COGNITIVE AND NEUROANATOMICAL CHANGES OVER FIVE YEARS IN GBA-POSITIVE PARKINSON’S DISEASE PATIENTS

Michela Leocadi1,2, Elisa Canu2, Giulia Donzuso3, Tanja Stojkovic4, Silvia Basaia2, Nikola Kresojevic4, Iva Stankovic4, Noemi Piramide1,2, Aleksandra Tomić4, Vladana Markovic4, Igor Petrovic4, Elka Stefanova4, Vladimir Kostic4, Federica Agosta1,2,5, Massimo Filippi1,2,6

1Vita-Salute San Raffaele University, N/a, Milan, Italy, 2IRCCS San Raffaele Scientific Institute, Neuroimaging Research Unit, Division Of Neuroscience, Milan, Italy, 3University of Catania, Department “g.f. Ingrassia”, Section Of Neurosciences, Catania, Italy, 4University of Belgrade, Clinic Of Neurology, Faculty Of Medicine, Belgrade, Serbia, 5IRCCS San Raffaele Scientific Institute, Neurology Unit, Milan, Italy, 6IRCCS San Raffaele Scientific Institute, Neurology Unit, Neurorehabilitation Unit And Neurophysiology Service, Milan, Italy

Background and Aims:: To study the longitudinal disease course of Parkinson’s disease (PD) patients with glucocerebrosidase (GBA) mutation (GBA-positive) compared to PD noncarriers (GBA-negative) along a five-year follow-up.

Methods:: Ten GBA-positive and 20 GBA-negative PD patients underwent clinical, neuropsychological and MRI assessments (cortical thickness and subcortical, hippocampal and amygdala volumes) at study entry and once a year for five years. At baseline and at the last visit, each group of patients was compared with 22 age-matched healthy controls. Clinical, cognitive and MRI features were compared between groups at baseline and over time.

Results:: At baseline, GBA-positive and GBA-negative PD patients had similar clinical and cognitive profiles. Compared to GBA-negative and controls, GBA-positive patients showed cortical thinning of left temporal, parietal and occipital gyri. Over time, compared to GBA-negative, GBA-positive PD patients progressed significantly in motor and cognitive symptoms, and showed a greater pattern of bilateral cortical thinning involving also frontal cortices. After five years, compared to controls, GBA-negative PD patients showed a pattern of cortical thinning similar to that showed by GBA-positive cases at baseline. The two groups of patients showed similar patterns of subcortical, hippocampal and amygdala volume loss over time.

Conclusions:: Compared to GBA-negative PD, GBA-positive patients experienced a more rapid motor and cognitive decline together with a greater, earlier and faster cortical thinning. Cortical thickness measures may be a useful tool for monitoring and predicting PD progression in accordance with the genetic background. Funding: Ministry of Education and Science of the Republic of Serbia (Grant #175090).
HD LIKE PRESENTATION OF HIV IN ADULT: RARE CASE REPORT

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**Background and Aims:** Movement disorders including parkinsonism, tremor, myoclonus, and dystonia have been reported in patients with HIV (human immunodeficiency virus) encephalopathy. Chorea and ballismus have been reported in AIDS (acquired immune deficiency syndrome) complicated by CNS toxoplasmosis infection. Huntington disease (HD) is common cause of chorea in adult with chronic history. Generalised chorea as a presenting symptom of HIV rare. We are reporting this HD like presentation of HIV in adult as it is probably the rare case report after thorough review of literature.

**Methods:** A 54-year-old male presented with 1.5-year history of generalized hyperkinetic movement involving face, limb and trunk with 1 year history of behavioural symptoms in the form increased irritability and impulsivity. Family history was negative. Neurological examination showed generalized chorea involving upper face, peri-oral region, tongue, limb and trunk with frontal dysfunction. Rest of examination was unremarkable.

**Results:** On evaluation, all blood investigation including blood glucose, renal function test, serum electrolytes, thyroid function test and ceruloplasmin were normal. Peripheral smear’s for acanthocyte were negative. MRI brain showed bilateral moderate caudate atrophy. Genetic study for HD negative. He tested positive for HIV.

**Conclusions:** This case highlights that HIV can present with typical HD phenotype clinically as well radiologically in adult. It should be considered in differential diagnosis of patients without genetic etiology.
HEMI-CHOREA-BALLISM; AN UNCOMMON PRESENTING PHENOMENOLOGY IN WILSON’S DISEASE

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National Hospital of Sri Lanka, Institute Of Neurology, Colombo, Sri Lanka

Background and Aims:: Hemi chorea – ballism is usually seen in the elderly, secondary to stroke and uncontrolled diabetes. It is an uncommon phenomenology in the young, especially without a structural brain pathology. We describe a case of a young girl presenting with hemi chorea with normal brain imaging secondary to neuro Wilsons disease (WD).

Methods:: Case Report A 16 year old girl presented with left hemi chorea involving both upper and lower limbs over a period of one week. She had no movement abnormality elsewhere. She was cognitively normal with no emotional lability. History of sore throat two weeks prior was noted along with symmetrical small joint arthritis. Except for the hemi chorea neurological examination was normal.

Results:: 2D echocardiogram revealed grade two mitral regurgitation. Her hematology including an auto immune screen, thyroid function, inflammatory markers were normal. However elevated ASOT 800IU/ml was detected. Copper screen showed an elevated 24 hour urinary copper (2.89 umol/24 hours (0.23-1.09), with a normal serum caeruloplasmin level. Subsequently bilateral KF rings were detected on slit lamp. Genetic confirmation with ATP 7 B mutation for WD is awaited. Copper chelation therapy with penicillamine was initiated resulting in near complete resolution of the movement abnormality.

Conclusions:: Hemi chorea in childhood is an exceptionally rare movement phenomenology especially without a structural brain lesion. Sydenham chorea is more generalised and bilateral. High ASOT level seen in this patient could occur in recurrent sore throat. Although WD can present with most types of movement disorders hemi chorea as a presenting feature is rarely described.
SEX-SPECIFIC WHOLE-BRAIN NETWORK TOPOLOGIC ORGANIZATION IN DRUG NAÏVE PARKINSON’S DISEASE PATIENTS

Sara Satolli¹, Federica Agosta², Rosa De Micco¹, Silvia Basaia², Mattia Siciliano¹, Camilla Cividini², Gioacchino Tedeschi¹, Massimo Filippi², Alessandro Tessitore¹
¹Università degli studi della Campania "Luigi Vanvitelli", Department Of Advanced Medical And Surgical Sciences, Napoli, Italy, ²IRCCS San Raffaele Scientific Institute, Neuroimaging Research Unit, Division Of Neuroscience, Milan, Italy

Background and Aims:: Compelling evidence suggests that a gender-specific pattern and functioning within the nigrostriatal dopaminergic pathway may underlie different outcomes in patients with Parkinson’s disease (PD). We aim to investigate the potential effect of sex on the whole-brain network topologic organization in a cohort of drug-naïve PD patients using resting-state functional MRI and correlations with baseline and longitudinal clinical features.

Methods:: 3T MRI images of 147 drug-naïve PD patients (85/62 male/female), and 38 controls (20/18 male/female) were acquired. Graph analysis and connectomics were used to assess global and local topological network properties and regional functional connectivity (FC) in female PD patients compared to males. Multivariate linear and logistic regressions investigated whether functional imaging data at baseline were predictors of clinical outcome over a 4-year period.

Results:: At 4-year follow-up, female PD patients were more likely to present treatment-related motor complications, especially dyskinesia. At baseline, female PD patients showed a preserved global functional brain architecture compared to controls. Male PD patients showed altered functional topological properties within the basal ganglia network compared to female PD patients. No FC differences were detected between male and female controls. Functional connectivity changes within the basal ganglia at baseline were correlated with risk of motor complications at follow-up.

Conclusions:: Our findings revealed the presence of a disease-related, sex-specific functional basal ganglia architecture in a cohort of early PD patients. These findings may be related to the presence of different gender-specific nigrostriatal dopaminergic pathways and might be potentially used to predict disease progression over time.
ALPHA-SYNUCLEIN PATHOLOGY AND ENTERIC GLIA IN ADVANCED PARKINSON’S DISEASE: A STUDY FROM GASTROINTESTINAL BIOPSIES

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Background and Aims:: In Parkinson’s Disease (PD), recent evidence points towards the involvement of gut-brain axis as one of the primary physio-pathological mechanisms underlying α-Syn aggregation and propagation to CNS. Furthermore, gastrointestinal dysfunctions represent one of the main non-motor symptoms in PD, often preceding the development of proper motor symptoms. Our aim was to investigate the enteric nervous system (ENS) in PD by characterizing α-Syn alterations and glial responses in stomach-duodenum biopsies of PD patients.

Methods:: 16 patients with advanced PD which underwent Duodopa Percutaneous Endoscopic Gastrostomy and Jejunal Tube (PEG-J) placement were included in the study. A mean of 4 (2mm3) wall biopsies were sampled from each patient. Immunohistochemistry was performed with anti-aggregated-α-Syn (5G4) and GFAP antibodies. The presence of phospho-α-Syn in conjunction with βIII-tubulin was investigated by immunofluorescence. Morphometrical-semi-quantitative analysis was performed to characterize 5G4+ and GFAP+ density and size. Duodenal control biopsies were included from 8 age-and-sex-matched patients undergoing routine diagnostic endoscopy.

Results:: Elevated immunoreactivity for both phosphorylated and aggregated α-Syn was identified in all biopsies of PD patients compared to controls. Immunohistochemistry was performed with anti-aggregated-α-Syn (5G4) and GFAP antibodies. The presence of phospho-α-Syn in conjunction with βIII-tubulin was investigated by immunofluorescence. Morphometrical-semi-quantitative analysis was performed to characterize 5G4+ and GFAP+ density and size. Duodenal control biopsies were included from 8 age-and-sex-matched patients undergoing routine diagnostic endoscopy.

Conclusions:: The ENS could be one of the earliest implicated structures in the patho-physiology of PD. The analysis of enteric glia could represent a precocious biological marker of the disease, as its responses to pathological α-Syn could unveil a link between gastrointestinal neural and immune systems in PD inflammation.
LONG-TERM CLINICAL, NEUROPHYSIOLOGICAL AND NEUROIMAGING FOLLOW-UP OF A PATIENT WITH HEMIPARKINSON-HEMIATROPHY SYNDROME

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Background and Aims:: Hemiparkinsonism-hemiatrophy syndrome (HPHA) is a rare form of secondary parkinsonism characterized by unilateral body atrophy associated to early onset ipsilateral parkinsonism, with slow progression, inconstant contralateral involvement and variable response to levodopa. For the first time, we describe a long-term clinical and instrumental follow-up of a patient with HPHA.

Methods:: Case report: a 16-year-old male developed a gradually worsening mild slowness and stiffness of left limbs. At age 19, he showed slight rigidity, bradykinesia and distal dystonic posturing on his left side (UPDRS-III motor scores: 30) and mild ipsilateral somatic atrophy. Longitudinal assessment: at baseline, neurological examination after L-Dopa administration, brain MRI, [123I]-FP-CIT DAT-SCAN, genetic analysis for PINK1 and PRKN gene, transcranial magnetic stimulation (TMS) before and after DOPA; during the 18-year follow-up: repeated clinical assessments and instrumental evaluations (i.e. neuroimaging after 15 years, yearly TMS during the first four years).

Results:: At baseline: 1. unremarkable brain MRI; 2. negative genetic analysis; 3. bilateral asymmetric (right-left) decrease of striatal transporter binding on DAT-SCAN; 4. significant clinical improvement (UPDRS-III: 11) after 200-mg oral levodopa; 5. reduced TMS short intracortical inhibition in the right hemisphere, unmodified after levodopa. Diagnosis of HPHA syndrome was confirmed and rotigotine, 4 mg/die, was started with clinical improvement. Neurological exam showed a slight worsening of limb dystonia in the 18 years of follow-up (UPDRS-III: 32). No changes were found on TMS, brain MRI and DAT-SCAN.

Conclusions:: The present long-term multimodal clinical and instrumental assessment confirmed the slow clinical progression of HPHA, whereas structural/metabolic brain damages and neurophysiological findings remained unchanged.
TEST-RETEST RELIABILITY OF STATIC POSTURAL BALANCE VARIABLES IN NATURAL AND FEET-TOGETHER STANCE CONDITIONS

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Background and Aims:: The aim of this study was to investigate the test-retest reliability of postural balance variables during the natural and feet-together stance conditions. It is important to confirm the reliability of postural balance variables because the results of balance tests would be different with different balance test protocols, i.e., stance conditions such as natural and feet-together stances.

Methods:: Sixteen young healthy adults were instructed to sustain their center of body mass as stably as possible on the force plate. As balance standing conditions, natural (a comfortable self-selected stance width) and feet-together stances (placing the feet 0’ apart) were selected. The mean distance, mean velocity, mean frequency, and 95% confidence ellipse area were derived from the center of pressure (COP) time series in the overall, anteroposterior (AP), and mediolateral (ML) directions. To evaluate the test-retest reliability of the postural balance variables, Cronbach’s alpha coefficient was calculated in each stance condition.

Results:: Mean velocity was the most reliable variable particularly in three times balance test with in both the natural and feet together stances (α = 0.805 – 0.921). The reliability of all variables of three times balance test was greater than that of twice balance test , mainly in the natural stance. In contrast, the mean ML distance of the feet-together stance had poor reliability despite three balance tests (α = 0.243).

Conclusions:: These results suggest that the balance test protocol should consider the appropriate stance conditions as well as the number of balance trials to select the reliable postural balance variables.
Background and Aims:: Complex Regional Pain Syndrome (CRPS) is a chronic inflammatory disease severely disabling also characterized by neurological complications. Dystonia and dystonic tremor may occur in the chronic phase of CRPS, however movement disorders associated with CPRS are often underrecognized. Here we report a case series of 3 patients with dystonias associated with CRPS.

Methods:: Cases. The first one was a young man of 18 years of age who developed CRPS after a traumatic injury to the right forearm. Dystonic posture with adducted arm, flexed forearm and pronated hand occurred after 13 months from CRPS onset. The second patient was a 66 year-old female patient who progressively developed a dystonic tremor and dystonia of the left arm after 12 months time of pain, swelling and cutaneous allodynia in the same limb. The third patient was a 46 year-old male who developed dystonia of left limbs after a 12-month period with recurrent pain and swelling of the left hand and foot. All patients underwent intravenous treatment with neridronate.

Results:: All patients had clinical improvement and reduction of CSS scores after treatment with neridronate. The first two patients had complete regression of pain and dystonia with complete restoration of limb range of motion. The third patient showed a partial improvement of dystonic postures.

Conclusions:: Our data indicate that dystonias due to CRPS if treated early could have a complete remission. Physicians should be aware that CRPS may be associated with treatable dystonia in the chronic phase of the disease.
PARKINSON’S DISEASE RISK FACTORS AND AGE

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Background and Aims:: Objective: Aim to study some risk factors in patients with Parkinson disease (PD).
Methods:: It was a retrospective analysis conducted in the Department of Neurology, Third Central Hospital of Mongolia from January 2016 to December 2019. We assessed 71 patients history with PD. They were diagnosed according to criteria of The United Kingdom Parkinson’s Disease Society Brain Bank clinical diagnostic criteria (UKPDSBB).
Results:: Total 71 patients (female 82.3%) enrolled in this study. The respondents 29.7% are at the age of 40-59 years, 70.3% are above the age of 60 and the average age is 65.6±7.3. Age at onset of sign of the PD was divided into three group: 3.5% at below 39 years, 45% at 40-59 years, 51.5% at more than 60 years. Average age is 58.6±9. We compared the age at onset of sign and some risk factor that in the middle age they had trauma of brain in 26.8%, combined factor in 53.5%, and in the old age diagnosed with patient they had metabolic in 5.1%, psychiatric disorder in 8.2% environmental factors in 6.7%, vascular disorders in 47.4% and concomitant disorders in 32.6%. About 6% of patients have a family history of PD.
Conclusions:: Risk factors for PD are more likely to be age-related vascular disorders and middle-aged brain injury. The age of the respondent and the age at which the onset of the disease (age at which the onset of the first symptoms appeared) accounted ages over 60, and the clinical symptoms became more advanced with age.
STRUCTURAL GRAY AND WHITE MATTER LONGITUDINAL ALTERATIONS IN PARKINSON’S DISEASE WITH REM SLEEP BEHAVIOR DISORDER

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Background and Aims:: In Parkinson’s disease (PD), the presence of REM sleep behavior disorder (RBD) is associated with cortical and subcortical abnormalities. We aimed to longitudinally investigate structural differences in patients with PD, according to the presence of RBD.

Methods:: 153 PD patients underwent clinical assessment, neuropsychological evaluation and Magnetic Resonance Imaging (MRI) scan once a year up to 48 months. Patients were classified as RBD+ (n=45) or RBD- (n=108) according to RBD-questionnaire scores (cut-off = 5). Cortical thickness and deep nuclei volumetry were assessed at each timepoint. Moreover, white matter hyperintensities (WMH) were identified on T2-weighted images and WMH total volume was computed for each scan. Clinical and cognitive variables, gray matter (GM) and WMH volumes at baseline were compared, and their longitudinal progression was investigated with age-adjusted linear mixed-effects models.

Results:: At baseline, RBD+ PD patients were older, showed worse global motor and cognitive performance, higher WMH volume and higher degree of atrophy in frontal, temporal and occipital areas, as well as bilaterally in basal ganglia. Longitudinally, the RBD+ group showed worse longitudinal progression in motor and cognitive performance, WMH volume and atrophy in thalami and accumbens nuclei bilaterally, left nucleus pallidum and right putamen compared to RBD- group.

Conclusions:: Our study showed extensive brain alterations in both GM and WM in PD patients with RBD, with more evident clinical, cognitive and structural MRI alteration worsening over time, suggesting more rapid neurodegeneration in PD with RBD. Funding: Ministry of Education and Science Republic of Serbia (Grant #175090).
NEW PRION PROTEIN MUTATION (T183S) WITH ATYPICAL PARKINSONISM AND GSS-LIKE NEUROPATHOLOGY.

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Background and Aims:: The Canadian CJD surveillance, active since 1998, has reported 1133 prion disease cases. The mortality rate of CJD in Canada averaged 1.96/1,000,000 over the past 5 years. 7% of the cases were genetic in origin.

Methods:: Case report

Results:: We report the case of an at death 78-year-old gentleman with three-year history of slowly progressive mild cognitive impairment, Parkinsonism (mainly bradykinesia), and vertical gaze palsy; poorly responsive to Dopa. He rapidly declined two months before his death with profound dementia, myoclonus, and akinetic mutism. An MRI showed subtle cortical restricted diffusion, EEG showed periodic triphasic waves, QuIC testing was negative, hTau positive, and 14-3-3 was borderline. Genetic testing revealed a T183S mutation of PRNP. Genetic testing of family members has not yet been performed.

Neuropathology revealed multicentric prion protein plaques (12F10) in the deeper neocortical layers, hippocampus, and the molecular layer of the cerebellum. Spongiosis was minimal and focal, and unassociated with plaques. The morphology is consistent with GSS or GSS-like prion disease. No PD or PSP neuropathological changes were present.

Conclusions:: The clinical presentation in this patient with T183S mutation is different from the CJD profile present in patients with T183A mutation. A similar dimorphic situation occurs with mutations on codon 232. T183S has similarities to the D202N mutation which also shows atypical Parkinsonism with GSS neuropathology (Plate et al, Mov Disord 2013; 28: 241-244). In the clinically challenging group of atypical Parkinsonism, it is good to consider a prion disease in the differential diagnosis, alongside more likely candidates such as PSP.
BRADYKINESIA IN PATIENTS WITH VALPROATE-INDUCED TREMOR

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Background and Aims:: Valproate is one of the most effective treatments for epilepsy. Among its side effects, tremor and parkinsonism have been reported. Earlier neurophysiological observations showed bradykinesia (movement slowness) during upper limb movement in patients with valproate-induced tremor. However, the pathophysiological mechanisms of this movement abnormality are unclear.

Objective: To investigate the possible occurrence of bradykinesia in patients with valproate-induced tremor during finger movements and possible distinguishing features with bradykinesia in Parkinson’s disease.

Methods:: 22 patients with valproate-induced tremor, 22 patients with Parkinson’s disease, and 22 healthy controls were enrolled. All participants underwent a standardized neurological examination, video recordings, and kinematic assessment of the finger tapping. Rest, postural and kinetic tremor of the upper limbs was also objectively recorded in patients using a motion analysis system. One-way analysis of variance was used for between-group comparisons. Correlations analysis was used to test possible correlations between clinical data and kinematic features in patients.

Results:: Clinical evaluation and kinematic analysis showed that patients with valproate-induced tremor were slightly bradykinetic, i.e. slower, than healthy controls (both p<0.05). Unlike Parkinson’s disease patients, however, patients with valproate-induced tremor did not present a decrement in amplitude (sequence effect) during finger tapping. Finally, there was no correlation between bradykinesia and tremor severity in patients.

Conclusions:: Bradykinesia (movement slowness) without decrement is a common motor feature in patients with valproate-induced tremor which may suggest distinctive pathophysiological mechanisms.
DEEP BRAIN STIMULATION IN MOVEMENT DISORDERS: 15 YEAR EXPERIENCE OF KING FAISAL SPECIALIST HOSPITAL & RESEARCH CENTER

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Background and Aims:: Deep brain stimulation is a revolutionary intervention that treats specific movement disorders through targeting particular areas in the brain. DBS offers hope for patients that do not reach sufficient benefit from medical management. King Faisal Specialist Hospital and Research Center has been providing DBS treatments since 2003 and has since provided the full spectrum of care surrounding the surgical and medical elements of implanting a DBS Device and monitoring the results through follow ups, programming and medical management support. The existence of this vast experience will serve as a reliable and detailed reference to navigate the decision, choice, management and follow ups for the use of DBS in movement disorders patients.

Methods:: a retrospective chart review of all the patients who underwent DBS in KFSH&RC with an aim to during the period of 2003 to 2020

Results:: The results currently under review will characterize indications, contraindications, complications, and disease response to DBS.

Conclusions:: Deep Brain Stimulation is a revolutionary intervention and has the potential to provide benefit for many patients, the review of a resourcesful and experienced tertiary healthcare center with a significant number of DBS procedures and follow ups would provide an indepth look on the spectrum of benefit provided by Deep Brain Stimulation for our patients.
IDENTIFICATION OF PARKINSON’S DISEASE BIOMARKERS THROUGH RNA SEQUENCING OF PERIPHERAL BLOOD LEUKOCYTES

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Background and Aims:: Identifying reliable biomarkers for early diagnosis and staging of Parkinson’s disease (PD) is a priority and a challenge in the field. Transcriptomics is becoming an important tool to investigate the potential of cells to adapt gene expression in different physiological and pathological states. However, only few studies have focused so far on transcriptomic profiling as PD biomarker, and research of such biomarkers in peripheral blood is particularly lacking. The aim of this study is to investigate gene expression changes occurring in peripheral blood leukocytes (PBL) as potential biomarkers of PD.

Methods:: Blood leukocyte samples were collected from four different groups of patients: early PD (EPD), advanced PD with dementia (PDD), Alzheimer’s disease (AD) and healthy volunteers as controls (CTR). RNAseq - MACE (Massive Analysis of cDNA ends) has been performed on available samples to obtain an unbiased landscape of transcript expression changes between patients and controls.

Results:: Our high throughput analysis has enabled us to identify a number of genes that are most upregulated/downregulated in the patients’ PBL and which are specific for any disease condition (EPD, PDD, or AD) (Figure 1-3). Importantly, we detected several gene expression changes that could represent potential biomarkers for PDD (1055), EPD (328) and AD (400).
Conclusions:: Validation studies of the top-ranking candidate genes are currently ongoing by recruiting new independent cohorts of patients. The results of the present study seem to be promising in the short/mid-term challenge to improve PD diagnosis, assess disease severity, and prognosticate course of disease.
COGNITIVE OUTCOME FOLLOWING BILATERAL SUBTHALAMIC NUCLEUS DEEP BRAIN STIMULATION IN PARKINSON’S DISEASE: A COMPARATIVE OBSERVATIONAL STUDY IN THE INDIAN POPULATION

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Background and Aims:: The improvement in motor outcomes after bilateral subthalamic nucleus deep brain stimulation (STN DBS) has been well established in patients with Parkinson’s disease (PD). However, the cognitive changes related to STN DBS are debatable, with studies showing divergent results.

Methods:: We conducted a prospective comparative observational study to assess the effects of bilateral STN DBS on cognition at minimum two years of neurostimulation when compared to a group of patients with PD on medical management alone. 34 patients in each group were compared for various neuropsychological scores. The two groups were matched for age, severity of disease, LEDD at baseline and duration of PD.

Results:: At a mean follow up of around 33 months, we found a significant decline in verbal fluency scores in the DBS group, and a trend for decline was noted in digit span test, both measures of frontal executive function. Though other cognitive scores declined over time in each group, there was no difference between the surgical and medically managed groups, indicating that these were attributable to the natural progression of PD.

Conclusions:: Our study demonstrated impairment in the selective cognitive task of verbal fluency and a trend towards impairment in attention, with no other major significant neuropsychological outcomes attributable to STN DBS. We postulate that these effects on fluency and attention are attributable to STN stimulation and modulation of the fronto-striatal circuits. DBS of STN can be considered safe from the cognitive viewpoint in patients with idiopathic Parkinson’s disease.
BIBLIOGRAPHIC REVIEW OF THE ALTERATION IN THE ELEMENTS OF MOVEMENT HUMAN IN PERSONS WITH MULTIPLE SCLEROSIS

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Background and Aims:: The Multiple Sclerosis is a disease with affection of diverses elements of human movement for the process of affection of myelin and in this context exist impacts in the tone, coordination, balance, posture and sensibility that in the evolution of diseases have negative implications in the chronic and progressive course of disease for the functionality and the interaction of the persons with the environment

Methods:: This investigation is a bibliographic review around alteration in the elements of human movement in multiple sclerosis, the data base was Sciences Direct, Ebsco, Pubmed, and Elsevier, the key words in the search was multiple sclerosis and human movement alterations, multiple sclerosis and functionality and the criterias of selection was original article with full text with publication in the last 10 years

Results:: In the investigation has 12 Articles, of this 7 was experimental study, 3 was no experimental studies, 1 was correlational study, an 1 article was analytic study. The principal elements with negative implications was the tone, sensibility, functional capacities, posture, coordination, balance, gait and endurance

Conclusions:: The principal implications in the human movement for the multiple sclerosis for alterations in the myelin are in the tone that generate negative impacts for the functional capacities, posture, balance and gait and in this points are more big the alterations for the problems in the coordination producing a interaction in the problems of tone and the coordination for the human movement in persons with multiple sclerosis in the progressions of diseases
THE PROGNOSTIC VALUE OF G325R GBA MUTATION ON THE LONG-TERM DEEP BRAIN STIMULATION OUTCOME IN PARKINSON’S DISEASE

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Background and Aims:: GBA mutations are the most common genetic risk factor for Parkinson’s disease (PD), which are typically observed in younger and cognitively more impaired individuals. However, only a few GBA variants described in PD (n=130) have been associated with patients’ clinical phenotype. We describe here the case of a rare GBA mutation who was followed-up for over 20 years.

Methods:: A 32-year-old lady was diagnosed with early-onset PD in 1998 for the presence of rigidity, bradykinesia, constipation, and episodic urinary incontinence. Five years later she developed severe motor fluctuations for which, in 2007, she underwent bilateral subthalamic Deep-Brain-Stimulation (DBS) surgery. She was genetically screened using an extensive panel.

Results:: DBS resulted in remarkable improvement of both motor and nonmotor PD symptoms. Two years after lead implantation, in 2009, our patient developed psychiatric symptoms for which she received a diagnosis of bipolar disorder. Nonetheless, psychiatric symptoms remained well compensated over time. Fourteen years after DBS, motor symptoms and complications were still well controlled, apart from mild dyskinesia, and there was no evidence of cognitive decline on neuropsychological testing. Genetics revealed the presence of heterozygous GBA mutation c.1090G>A–p.(Gly364Arg) (G325R), which was previously reported in severe forms of Gaucher disease and in a single case of PD.

Conclusions:: In contrast to most common GBA variants, G325R, albeit infrequent, associates with a benign disease course and long-lasting response to DBS. Although the underlying neurobiological mechanisms remain to be clarified, the prognostic value of different GBA variants should be analyzed to inform prognosis and response to DBS.
MOVEMENT DISORDERS RELATED TO PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA: 
TWO NOVEL CASES AND A LITERATURE REVIEW

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Background and Aims:: Primary CNS Lymphoma (PCNSL) is a rare and aggressive extranodal non- 
Hodgkin lymphoma (NHL), occurring either in immuno-deficient or immuno-competent subjects. It is often 
located in subcortical areas, often accounting for motoric disorders. Here, we reviewed PCNSL-related 
 movement disorders (MDs), outlining the main features, in order to improve the clinical management of 
the condition.

Methods:: We conducted a retrospective analysis on a cohort of patients with PCNSL presenting with 
MDs, including all existing cases identified by a systematic literature review (source: Medline; period: 
1946-2020) and two unreported cases. Data on phenomenology, neuroimaging, pathology, and clinical 
course were collected.

Results:: We included 13 patients from eleven previous reports and two novel unreported cases from our 
center, for a total of 15 subjects. We observed that the most frequent PCNSL-related MD was a 
parkinsonian syndrome, appearing at about 60 years of age, unresponsive to levodopa, associated with 
other neurological signs. Chorea, dystonia, and dyskinesia were rarer, and presented some degree of 
responsiveness to symptomatic treatments. PCNSL was localized in basal ganglia in most cases. MDs 
often ameliorated after tumor mass reduction.

Conclusions:: This study defined the main features of PCNSL-related MDs, providing useful clues 
especially to early diagnose the disease. In fact, since the therapeutic scenario of PCNSL is changing, a 
timely diagnosis is crucial to ensure adequate treatments to patients.
ANALYSIS OF DYSGRAPHIA IN ADVANCED PARKINSON’S DISEASE PATIENTS FOLLOWING BILATERAL STN-DBS – A PROSPECTIVE STUDY

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Background and Aims:: Parkinson’s disease is characterized by varying intensities of bradykinesia, rigidity and tremor leading to disturbances in writing skills of the patient. We undertook this study to evaluate dysgraphia features in advanced Parkinson’s disease cases and changes in these features after bilateral Subthalamic Nucleus Deep Brain Stimulation.

Methods:: All idiopathic PD cases who underwent DBS at our centre were included in this study. Patients were assessed preoperatively for dysgraphia by analysis of handwriting in OFF phase by a single investigator on bedside testing. For quantification of micrographia, vertical length of first letter and width of the word written was calculated. An analysis of legibility of handwriting was also done for all patients using Fahn-Tolosa-Marin Tremor Rating Scale (FTMTRS). Patients were analysed for dysgraphia at 6 months post-surgery in Drug OFF phase and outcomes were correlated with baseline parameters.

Results:: There were a total of 51 patients who were included in our study. Significant reduction was noted in postoperative UPDRS III scores (P = 0.0001). Age more than 65 years was associated with less improvement in FTMTRS Scores. Prevalence of micrographia reduced in postoperative period, but the difference was not statistically significant. Mean FTMTRS score in preoperative OFF phase and postoperative OFF phase was 2.38 + 0.74 and 1.61 + 1.03 respectively. Difference in pre and post-surgery FTMTRS scores was found to be statistically significant (P =0.0001).

Conclusions:: Subthalamic Nucleus Deep Brain Stimulation results in substantial improvement in handwriting skills of patient particularly in cases with age less than 65 years.
COMMON FACTORS REDUCING SLEEP QUALITY OF PATIENTS WITH PARKINSON’S DISEASE IN KYRGYZSTAN.

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Background and Aims:: Patients with PD often suffer from sleep disorders, which may be caused by nocturnal symptoms, early morning symptoms, painful leg cramps, vivid dreams, nightmares, etc. Aim is to identify common factors that reduce sleep quality in patients with Parkinson’s disease (PD) in Kyrgyzstan.

Methods:: 29 PD patients participated in the survey, conducted at movement disorder clinic in Bishkek, 18 males and 11 females. The mean age was 66.59+/−8.753(48-85) years. Pittsburgh Sleep Quality Index (PSQI) questionnaire was used in the paper-based study.

Results:: Most of participated patients indicated sleep disturbances (93%), while only 2 of the 29 respondents had optimal sleep indices (4 points). Some responses showed a discrepancy between the subjective sleep assessment and their total PSQI score. Thus, 86% patients with a score over 5 points assessed the quality of their sleep as “fairly good”. Figure 1 shows the overall results of each patient who participated in the study.

Table 1 indicates a detailed analysis of PSQI component #5 responses, where the most common sleep issues are waking up in the middle of the night or early morning (69%), waking up for using the bathroom (66%), failing to fall asleep within 30 minutes (45%).
Only 21% of the patients indicated having breathing problems, and 31%—sleep problems associated with pain during the past month period. **Conclusions:** Sleep disturbances affect the majority of participated PD patients. Sleep problems are caused mainly by early morning symptoms, nocturnal symptom, and trouble with falling asleep, directly affecting the amount and quality of sleep. Further study of the matter is crucial due to its influence on patients’ quality of life.
RESCUE OF STRIATAL LONG-TERM DEPRESSION BY CHRONIC MGLU5 RECEPTOR NEGATIVE ALLOSTERIC MODULATION IN DISTINCT DYSTONIA MODELS

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Background and Aims:: An impairment of long-term synaptic plasticity is a peculiar endophenotype of distinct forms of dystonia. We previously demonstrated a complete loss of corticostriatal long-term synaptic depression (LTD) in rodent models of two distinct isolated dystonias, resulting from mutations in the TOR1A (DYT1), and GNAL (DYT25) genes. Broad-spectrum antimuscarinic drugs are used to counteract abnormal striatal acetylcholine-mediated transmission, which plays a crucial role in dystonia pathophysiology. The aberrant excitability of striatal cholinergic cells can also be modulated by group I metabotropic glutamate receptor subtypes. Here, we tested the efficacy of the negative allosteric modulator of mGlu5 receptor (dipraglurant) on striatal LTD.

Methods:: Tor1a¹/∆GAG mice and GNAL¹⁻⁰⁻⁻ rats were randomly divided into four groups and injected intraperitoneally with either dipraglurant (50 mg/kg) or vehicle (ringer lactate) for 7 days. Then, the animals were sacrificed for electrophysiological recordings of striatal spiny projection neurons (SPNs), performed through conventional sharp technique.

Results:: Whereas acute treatment failed to rescue LTD, chronic dipraglurant rescued this form of synaptic plasticity both in DYT1 mice and GNAL rats. The pharmacokinetic profile of dipraglurant revealed a relatively short half-life, uncovering a peculiar time-course of recovery based on the timing from last dipraglurant injection. Indeed, SPNs recorded within 2 hours from last administration showed full expression of LTD, whilst the extent of recovery progressively diminished when SPNs were recorded 4-6 hours after treatment.

Conclusions:: Our findings suggest that distinct dystonia genes may share common signaling pathway dysfunction and that dipraglurant might be a potential novel therapeutic agent for this disabling disorder.
DEFINITION OF PARKINSON’S DISEASE AND ESTIMATION OF ITS INCIDENCE BASED ON NATIONWIDE PRESCRIPTION- AND DIAGNOSTIC DATA

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Background and Aims:: Health registers that cover entire Nordic nations present a valuable source of data for epidemiologic research. However, identification of incident cases based on register data is especially challenging for Parkinson disease (PD) due to the lack of a clinical gold standard and the existence of diseases with similar symptomatology. Some registered PD diagnoses may therefore be erroneous. Similarly, records of filled antiparkinsonian medicines may reflect other treatment indications or testing the presence of PD pathology. Our aim was to validate and facilitate the use of Norwegian Prescription Database (NorPD) and Norwegian Patient Registry (NPR) in epidemiologic research on PD by evaluating the congruence of information in these registers and by suggesting algorithms for identifying probable PD patients. The incidence of PD in Norway is also estimated.

Methods:: Cohen's Kappa and receiver operating characteristic (ROC) analysis with Youden index were employed.

Results:: The number of PD diagnoses and levodopa prescriptions were highly mutually predictive. Specificity of 0.90 and sensitivity of 0.92 were obtained when identifying individuals with >= 4 primary PD diagnoses based on having filled >= 4 levodopa prescriptions. The annual incidence rate corresponded to those generally reported in countries with similar demographic structure.

Conclusions:: The high correlation between diagnoses and prescriptions most likely reflects the process of testing treatment efficacy to verify the diagnosis. It also suggests the sufficiency of selecting PD patients based on information from either register alone in future studies. A clinically well-defined patient cohort is needed for further validation.
THE NEUROPROTECTIVE EFFECTS OF GINKGOLIDE K ON MPTP MICE

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Background and Aims:: Ginkgolide K (GK), a natural product isolated from Ginkgo biloba, exhibited an ability to promote the clearance of α-synuclein in A53T mutation cells, implying it may be a potential agent for Parkinson’s disease. However, it has not been reported whether GK can protect MPTP-induced dopaminergic neuron damage. Our aim was to observe the therapeutic potential and possible mechanisms of GK for protecting dopaminergic neurons through MPTP-induced PD model.

Methods:: PD model was induced by intraperitoneal injection of MPTP into male C57BL/6 mice, followed by GK treatment (20 mg/kg/day) for 7 consecutive days at the end of modeling. The motor coordination in mice was measured with the DigiGait system. The brain histopathological changes were determined by immunofluorescence staining. Peripheral immune changes of T cells and α-synuclein antibody were observed by flow cytometry and ELISA respectively.

Results:: GK ameliorated the gait dysfunction and dopaminergic neuron loss when mice were upon acute MPTP exposure. Simultaneously, GK switched microglia to M2 phenotype and decreased the microglia-mediated inflammation. GK treatment also inhibited peripheral CD4⁺IFN-γ⁺ and CD4⁺IL-17⁺ T cells and α-synuclein specific autoantibodies in MPTP mice.

Conclusions:: GK exerts a protective effect on dopaminergic neurons, which is related to the regulation of microglia polarization, the inhibition of inflammatory response modified by microglia, and the suppression of peripheral immune responses. (NNSF of China 81473577, 81971194; The Key Laboratory of Medicinal Resources and Natural Pharmaceutical Chemistry of Ministry of Education, Shaanxi Normal University 2019004. Ma and Xiao are corresponding authors)
PROSPECTIVE ANALYSIS OF MOTOR MANIFESTATIONS FOLLOWING STN-DBS AND THEIR CORRELATION WITH ELECTRODE POSITION

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Background and Aims:: Deep brain stimulation (DBS) has been proven to be a safe, reversible, cost effective procedure for treatment of Parkinson’s disease. Final electrode position remains a significant factor in determining the outcomes of STN-DBS. This study aims to analyze the final lead position in three-dimensional plane and its effect on motor outcomes in cases operated for STN-DBS.

Methods:: Patients of advanced Parkinson’s disease who underwent bilateral STN DBS were prospectively followed for improvement in gross motor outcomes at 6 months. Postoperative outcomes were correlated with final electrode position.

Results:: A total of 64 Patients (128 leads) were analyzed. There were 47 (73.44%) males and 17 (26.56%) females. The mean age of the patients was 57.23 ± 9.70 years (Range 36-83 years). Patients who were less than 65 years of age at time of surgery had more significant reduction in UPDRS III (p = 0.02). Cases with medio-lateral deviation of left x less than 3 mm had significant reduction in UPDRS III (p = 0.05) and speech sub-scores (p = 0.05). Deviation less than 2 mm in left x was significantly associated with more than 50% reduction in gait sub-scores (p = 0.04). Optimal placement of right y electrode was significantly associated with reduction in UPDRS III in postoperative period (P = 0.02).

Conclusions:: Subthalamic nucleus deep brain stimulation results in significantly improved functional outcome particularly in patients with age less than 65 years. Accurate final electrode position in relation to proposed target is associated with maximum clinical benefit.
THE ROLE OF REPAIR GENES IN THE PATHOGENESIS OF PARKINSON'S DISEASE

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Background and Aims:: At least 14 genes are known to have mutations leading to the development of Parkinson’s disease (PD). The presence of modifying effects of a number of associated genes and environmental influences has been proved [Hamza et al.,2010]. The aim of our study was to research the association of repair genes with PD.

Methods:: Two groups were studied (homogeneous by gender, age): I – 109 patients with Parkinson’s disease (PwPD) (mean age: 66.3±9.6; onset age: 58.16±9.55; H&Y stages 1–4), II – demographically-homogeneous population control group without PD (433 people: 51% men; 49% women). Comparing groups of PwPD with a population sample provides a number of advantages, since when comparing with a population control, the probability of obtaining false-positive results is significantly less than when comparing samples of PwPD with healthy ones. The clinical and neuropsychological assessment was performed.

Results:: An associative analysis of 8 SNPs in genes encoding proteins of various repair systems was performed: TP53BP1 (rs560191), NBN (rs1805800, rs709816), MRE11 (rs473297), ATM (rs189037, rs1801516), MLH1 (rs1799977), PMS2 (rs1805321). Gene products NBN, MRE11, ATM, TP53BP1 participate in the repair of double-stranded DNA breaks; genes MLH1, PMS2 are involved in mismatch repair processes. Statistically significant differences between the group of PwPD and the population sample in the frequencies of alleles and genotypes were found for rs1805800 (gene NBN), rs1801516 (ATM), rs1799977 (MLH1), (p<0.001).

Conclusions:: Thus, the association of polymorphism of repair genes with the development of PD was revealed, which indicates their involvement in the development of neurodegenerative disease. It is necessary to study these relationships further in a larger sample of PD patients.
THE PROTECTIVE EFFECT OF GINKGOLIDE B ON MPTP-INDUCED PARKINSON MICE

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Background and Aims:: Parkinson's disease (PD) is caused by progressive loss of dopaminergic (DA) neurons in the substantia nigra pars compacta (SNpc). Ginkgolide B (GB) is an important active ingredient of Ginkgo biloba, and plays an important role in anti-oxidation and nerve protection. Our aim was to observe the therapeutic potential of GB in PD mode and explore its possible mechanism of action.

Methods:: In vitro cell experiment, SH-SY5Y cells were divided into control group, MPP+ group and GB group. In animal model, mice were divided into normal group, PD group and PD+GB group, in which mice received GB by intraperitoneal injection at the beginning of the second week for 7 consecutive days.

Results:: Compared with the control group, GB promoted the expression of TH in SH-SY5Y induced by MPP+. Compared with MPTP-PD mice, GB effectively relieved motor symptoms and increased TH+ expression in SNpc. Similarly, TH protein expression was enhanced in GB brain extracts. Immunohistochemical staining showed that GB inhibited the abnormal activation of microglia and astrocytes. Compared with the model group, GB inhibited the expression of TLR4 on microglia and astrocytes, decreased the expression of TNF-α, inhibited iNOS expression in activated microglia.

Conclusions:: GB inhibits DA neuron damage, improved the clinical symptoms of PD, which is related to the inhibition of microglia and astrocyte-mediated neuroinflammatory responses, and the polarization of M2 microglia. (NNSF of China 81473577, Open Projects of The Key Laboratory of The Ministry of Education 2019004 and Chinese Academy of Sciences 2020-MDB-KF-09, China Postdoctoral Science Foundation 2020M680912, Ma and Xiao are corresponding authors)
SPECTRUM OF MOVEMENT DISORDERS AMONG CHILDREN WITH SUBACUTE SCLEROSING PANENCEPHALITIS (SSPE): A CROSS-SECTIONAL STUDY

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Background and Aims:: Subacute sclerosing panencephalitis (SSPE) is a rare neurodegenerative disorder due to persistent mutant measles virus infection, affecting children and young adults. Although movement disorders are known to occur in SSPE, their spectrum is poorly described in literature. We aimed to assess spectrum of movement disorders associated with pediatric SSPE.

Methods:: We conducted a single-center cross-sectional study and enrolled consecutive children (1 month-18 years) with SSPE who fulfilled modified Dyken criteria. We collected demographic, clinical and laboratory features and modified Rankin score (mRS) and Jabbour stage at presentation. All children were exhaustively examined for movement disorders.

Results:: We enrolled 30 children (20 males; 66.7%). Median age at presentation and onset was 5.4 (range: 2.5-14) years and 4.65 (1.5-14) years. Median duration of illness was 3 (0.3-36) months. Median mRS at presentation was 4 (2-5) and Jabbour staging 2 (1-3). Presenting complaints included myoclonus (n=28; 93.3%), cognitive issues (26; 86.7%), recurrent falls (12; 40%), seizures (10; 30%) and ataxia (5; 16.7%). Of these, 13 (43.3%) patients demonstrated movement disorders other than myoclonus. These included chorea/athetosis (4; 13.3%), tremor (3; 10%), parkinsonism (3; 10%), dystonia (2; 6.7%) and repetitive behaviors (2; 6.7%). There were no significant differences in terms of age at onset, sex, duration of illness or non-movement disorder clinical features among children with SSPE with and without movement disorders.

Conclusions:: Movement disorders are a common clinical feature among children with SSPE. This possibility must be considered among children presenting with movement disorders, especially in combination with myoclonus and cognitive impairment.
HYDROXYFASUDIL AMELIORATES PARKINSON’ S DISEASE POSSIBLY THROUGH ANTI-INFLAMMATION AND NEUROPROTECTION

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Background and Aims:: Fasudil is effective in the treatment of Parkinson’s disease(PD). But its fast metabolism and narrow safety window limit the clinical application. Hydroxyfasudil, active metabolite of Fasudil in vivo, exhibits higher Rho kinase selectivity and longer half-period. Our aim was to observe the therapeutic potential of Hydroxyfasudil in PD, and explore its possible mechanisms.

Methods:: PD model was induced by intraperitoneal injection(ip) of MPTP into male C57BL/6 mice, which were divided into MPTP group, Hydroxyfasudil group. Hydroxyfasudil was injected (40mg/kg/day) for one week from the second week. The injection of saline was set up as control in a similar manner.

Results:: Hydroxyfasudil effectively improved the motor symptoms of PD mice, and resulted in a significant attenuation of dopamine cell loss. Hydroxyfasudil also reduced the cytokines TNF-α, IL-6, IL-1β which were produced by Lipopolysaccharide(LPS)-induced BV2 cells and bone marrow-derived macrophages in vitro. Meanwhile, Hydroxyfasudil inhibited inflammatory response with the transformation of inflammatory M1 to anti-inflammatory M2 microglia, decreased the activation of TLR4. Compared with the MPTP group, the astrocytes and neurons in the Hydroxyfasudil group expressed more BDNF and GDNF (p<0.05).

Conclusions:: Hydroxyfasudil reduces the loss of dopaminergic neurons in the substantia nigra and improves motor symptoms by inhibiting inflammation and promoting the secretion of neurotrophic factors. (NNSF of China 81473577, Open Projects of The Key Laboratory Of The Ministry of Education 2019004 and Chinese Academy of Sciences 2020-MDB-KF-09, China Postdoctoral Science Foundation 2020M680912, Ma and Xiao are corresponding authors)
SEXUAL DIVERGENCIES IN MONOAMINERGIC PROJECTIONS IN PARKINSON’S DISEASE: A 123I-FP-CIT SPECT STUDY

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Background and Aims:: Background: preclinical and clinical studies suggest sex as important modulator of Parkinson’s disease presentation and progression. No studies largely evaluate sexual dimorphism in monoaminergic pathways in healthy subjects and Parkinson’s disease. Purpose: To investigate sex differences in nigrostriatal and extrastriatal 123I-FP-CIT SPECT monoaminergic projections in healthy subjects and Parkinson’s disease (PD)

Methods:: Established PD patients and 123I-FP-CIT SPECT imaging entered the study. Differences in 123I-FP-CIT binding between male and female healthy subjects and PD patients were separately evaluated by using whole brain SPM analyses adjusting for the effect of age, UPDRS-III and disease duration.

Results:: One-hundred forty-nine PD patients and 77 controls entered the study and underwent 123I-FP-CIT SPECT imaging. SPM analysis revealed higher binding in female in basal ganglia (p=0.001) and thalamus (p=0.001) in controls and PD patients. Conversely, male subjects (patients as well as controls) showed higher binding in frontal lobes and brainstem (p=0.001) compared to females.

Conclusions:: Conclusion: Healthy subjects and PD patients have similar sexual dimorphisms in monoaminergic pathways, suggesting that the impact of sex on incidence and progression of PD is driven by constitutional dimorphism rather than disease-specific alterations in dopaminergic and serotonergic systems.
PAIN AND BIOMECHANICAL CHANGES IN PATIENTS WITH PARKINSON’S DISEASE.

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Background and Aims:: There are a lot of pain syndromes of different localization in patients with Parkinson's disease (PD). This issue dedicated to the investigation of the pathogenesis of pain in PD.

Methods:: The study involved 243 patients with Parkinson's disease at different stages. To study the phenomenon of pain and comorbid disorders biomechanical tests, visual-analogue scale, the scale of "Quality of Life" were made.

Results:: Pain syndromes were detected in 221 patients (90.9%) with PD. The pain in the back - in 137 (56.4%) cases, headache - in 93 (38.3%) cases, mix pain - in 57 (23.5%) patients. A direct correlation between the types of pain and disease duration was demonstrated. Intensity of back pain was 7.1 ± 0.6 points, headache - 5.3 ± 1.1 points, widespread musculoskeletal pain - 6.9 ± 0.7 points. In patients with stage 1 - 5.1 ± 0.6 points, second - 6.8 ± 0.8 points, and the third - 7.5 ± 0.3 points. Chronic pain - 59 (24.3%) persons. The growth of chronic pain increases with the duration PD the disease. Biomechanical changes: spinal scoliosis - 76.1%. Asymmetry (frontal and sagittal planes) - in 236 (97.1%) patients, a violation of posture in conjunction with a change in the symmetry of shoulder girdle, shoulder blades - 203 (83.5%) of participants.

Conclusions:: The pain has a significant negative impact on the course of Parkinson's disease and quality of life of these patients. It is shown that pathogenesis of pain is due to biomechanical changes, that indicates the need for correcting the biomechanical disorders.
ADULT ONSET SPORADIC CHOREA: A SINGLE-CENTRE RETROSPECTIVE STUDY

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Background and Aims:: Adult Onset Sporadic Chorea is a rare movement disorder due to several causes, including genetic, pharmacologic, metabolic and structural ones. Here we provided a retrospective analysis of adult patients with sporadic chorea admitted to a single Italian centre, in order to highlights those features that may assist in appropriate clinical management.

Methods:: 11071 medical charts of patients admitted to the Neurology Unit of Tor Vergata University Hospital (Rome, Italy) during a nine years long period (2012-2020) were reviewed, identifying 28 patients with Adult Onset Sporadic Chorea (genetic forms excluded). Data regarding phenomenology, diagnostic workup, aetiology, treatments, and long-term outcome from this cohort were collected and analysed.

Results:: Adult Onset Sporadic Chorea occurred more frequently in females and presented with an acute-subacute onset. Cerebrovascular diseases accounted for 68% of aetiology; further causes were structural brain lesions, autoimmunity and others movement disorders syndromes. Clinical course was mild, with spontaneous resolution or minimal disturbances in 82% of cases. Appropriate clinical examination alone allowed diagnosing the 14% of Adult Onset Sporadic Chorea, neuroimaging the 76% of them, and basic laboratory tests the 10%.

Conclusions:: This study described the main clinical features of adult patients with sporadic chorea, showing that the vascular aetiology was the most common and that females were most frequently affected. Although in the majority of cases Adult Onset Sporadic Chorea may run with mild clinical course and good response to symptomatic therapy, a fast diagnostic workup is essential to identify those threatening conditions requiring immediate treatments.
ACUTE ONSET HEMIBALLISMUS/HEMICHOREA DUE TO VARIOUS ETIOLOGIES: A CASE SERIES

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Background and Aims:: Chorea is irregular, non-rhythmic, involuntary movements that can spread from one part of the body to another for a short time. Ballismus, on the other hand, is characterized with high amplitude choreic movements in the proximal extremities. The mechanism of acute hemichorea/hemiballismus has not been clearly explained. It is generally caused by lesions in the contralateral subthalamic nucleus (STN) and its afferent and efferent connections. Although vascular causes are the most common etiology, toxic-metabolic, inflammatory, infectious, demyelinating, and drug-induced causes have also been reported. Our aim is to present 6 patients with hemiballismus and/or hemichorea.

Methods:: The clinical and laboratory findings of six patients who came to outpatient clinics of Bagcılar Training and Research Hospital were retrospectively evaluated.

Results:: A 59-year-old male patient with thalamic hemorrhage due to cerebral amyloid angiopathy, a 67-year-old male patient with nonketotic hyperglicemia, a 59-year-old male patient with hypertensive thalamic hemorrhage, a 72-year-old male patient with infarction of left parietal lobe, a 26-year old female patient with demyelinating disease, a 75-year-old male patient with a history of flu medication usage were presented with hemichorea and/or hemiballismus. Three patients was started haloperidol treatment and one patient levetiracetam. Two patients were not given additional medication for chorea. Three of six patient showed full recovery.

Conclusions:: Hemichorea and/or hemiballismus may occur acutely and may result from etiologies that may require early intervention. More studies are needed to understand the pathophysiology, and particularly on managing treatment-resistant conditions.
INTRINSIC FUNCTIONAL CONNECTIVITY CORRELATES OF RBD IN COGNITIVELY UNIMPAIRED DRUG-NAIVE PARKINSON’S DISEASE PATIENTS

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Background and Aims:: REM Behavioural Disorder (RBD) is characterized by lack of skeletal muscle atonia during REM sleep and affects around 50% of patients with Parkinson’s disease (PD). PD patients with RBD present an increased risk of worse motor progression and dementia. We investigated intrinsic brain intra and inter-network connectivity correlates of RBD in a cohort of cognitively unimpaired drug-naive PD patients and correlated neuroimaging findings to clinical and cognitive measures.

Methods:: 3T MRI images of 56 drug-naive PD patients (25 PD-RBD and 31 PD-no-RBD) were acquired. RBD presence and severity were assessed by means of a clinical interview and the RBD Screening questionnaire (RBDSQ). Single-subject and group-level independent component analysis was used to investigate intra and inter-network functional connectivity differences within the default mode (DMN), frontoparietal (FPN), salience (SN) and executive control (ECN) networks between patients sub-groups. Linear regression analysis was used to investigate correlations between imaging and clinical data.

Results:: Compared to PD-no-RBD patients, PD-RBD showed an increased SN and ECN connectivity, a decreased FPN connectivity and both an increased and a decreased DMN connectivity. This imaging pattern was correlated with both RBD severity and cognitive outcomes in PD patients.

Conclusions:: Abnormal intrinsic brain connectivity within and between the major neurocognitive networks may represent a potential neural correlate of RBD symptoms and severity in early PD patients. This aberrant connectivity is correlated with cognitive outcomes even in the absence of cognitive impairment and may potentially be proposed to develop a sensitive and early biomarker of dementia in PD.
SLEEP DISTURBANCES IN IDIOPATHIC PARKINSON’S DISEASE: RELATIONSHIP WITH AGE AT ONSET AND DISEASE DURATION.

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Background and Aims:: Sleep disorders (SDs) are a common and disabling non-motor symptom (NMS) of Parkinson’s disease (PD), mostly in the form of REM-sleep behavior disorder. The PRIAMO study demonstrated that SDs are more frequently reported in patients with longer disease duration. In this retrospective study, we investigated the relationships between the occurrence of SDs, age at onset and disease duration.

Methods:: Medical records from 308 PD patients referring to our Movement Disorder Service between 2015 and 2020 were screened for the presence of SDs. This was defined as a score ≥2 in item 2 of the PD-Non Motor Symptoms Scale (NMSS). Patients were divided according to age at onset of motor symptoms (<65 years, n=157; 65-74 years, n=110; >74 years, n=41) and disease duration (≤10 years, n=187; >10 years, n=121).

Results:: Patients with age at onset <65 years displayed higher prevalence of SDs compared to the other two groups (75% vs. 62% vs. 46%; p<0.001). This difference was still significant considering the subgroups of patients with a disease duration ≤10 years (72% vs.54% vs. 43%; p=0.007) while there was no difference across all three groups in patients with a disease duration >10 years (79% vs. 77% vs. 67%; p=0.78).

Conclusions:: SDs are more prevalent in early-onset compared with later-onset PD patients. This difference disappears with disease progression while overall prevalence increases with disease duration.
ADHERENCE TO DRUG TREATMENT IN PATIENTS WITH PARKINSON'S DISEASE: EVALUATION OF A BRAZILIAN COHORT

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Background and Aims: Aims: To verify adherence to treatment and to identify intervening factors related to treatment abandonment or non-compliance with therapeutic guidelines among patients with Parkinson Disease (PD).

Methods: Descriptive, quantitative, observational epidemiological study Interview and application of questionnaires in PD attended between January 2019-July 2019; review of medical records. Hoehn&Yahr and Schwab-England Scale and knowledge and degree of adherence to drug therapy: Morisky and Green (1986) and Evaluation instrument for medication intake were evaluated. Considered adherent according to Morisky score between 6-8 [Figure 1].
Results:: Eighty-nine patients were interviewed, mean age was 68.8 years, 50.6% women. Regarding schooling, 47.2% had up to 4 years of training, 36% up to 12 years, 13.5% with more than 12 years. All the interviewees were using antiparkinsonian drugs. All of them used Levodopa / benzeraside, the most common formulation being 400/100mg / day (53.9%); 28% Pramipexole, 32.5% Amantadine, 8% Rasagiline (1mg/day) and 4% Selegiline (10mg/day). 48.3% of the patients used two to three drugs [Figure 2]. According to the Morisky Score were considered adherents to treatment 40 (44.9%) [Table 1].

According to the Evaluation instrument for medication intake, 19 (21.3%) have positive attitudes to maintain their treatment. There was a significant relationship between drug adherence and patient age (p = 0.02) and treatment time (p = 0.01).

Figure 1: Morisky Medication Adherence Scale (1986) and Evaluation instrument for medication intake (validated for Brazil).
Conclusions:

Most PD patients in this study did not fully adhere to the drug treatment. Patients with the lowest adhesion rate were those with greater age and longer disease duration. Social and family aspects and motor impairment of the disease did not influence the treatment.

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<tr>
<td>High adherence</td>
<td>(&gt;8 points)</td>
<td>8 (2.2%)</td>
</tr>
<tr>
<td>Medium adherence</td>
<td>(6-8 points)</td>
<td>38 (42.6%)</td>
</tr>
<tr>
<td>Low adherence</td>
<td>(&lt;6 points)</td>
<td>49 (55%)</td>
</tr>
</tbody>
</table>

**EVALUATION INSTRUMENT FOR MEDICATION INTAKE**

| Positive attitude | 19 (21.3%) |
| Negative attitude | 70 (78.7%) |

Table 1. Results of adherence to pharmacological treatment according to the two scales applied.

Figure 2. Medications used by study patients. All patients used at least one presentation of Levodopa / benseradise.
FRONTAL CORTEX DEFICITS IN PARKINSON’S DISEASE PATIENTS VULNERABLE TO PAREIDOLIAS.

Gajanan Revankar1, Noriaki Hattori1, Yuta Kajiyama1, Tetsuya Shimokawa2, Tomohito Nakano1, Masahito Mihara3, Etsuro Mori1, Hideki Mochizuki1
1Osaka University, Neurology, Osaka, Japan, 2NICT, Osaka, Cinet, Osaka, Japan, 3Kawasaki Medical School, Neurology, Okayama, Japan

Background and Aims:: Parkinson’s disease (PD) patients susceptible to visual hallucinations experience prodromal events in the form of ‘pareidolias’. Pareidolias are visual phenomena wherein ambiguous forms appear meaningful due to incorrect perception. Here, we studied the brain and behavioral signatures of pareidolias that affect the fronto-parietal circuitry influencing visual processing.

Methods:: 21 PD patients and 10 age-matched healthy controls participated. Neuropsychological tests included evaluations for cognition, attention and executive functions. Pareidolias were evoked using a computerized noise pareidolia test with simultaneous EEG and eye-tracking measurement. PD patients were divided into those with pareidolias (N=10) and those without (N=11). Responses were evaluated ‘during’ and ‘preceding’ the presentation of stimuli. Eye movement behavior were measured using fixation metrics. EEG amplitudes were analyzed in the presaccadic phase. Finally, pre-stimulus EEG spectral connectivity were evaluated using graph networks.

Results:: PD patients with pareidolia were older and under-performed on neuropsychological tests. Eye-tracking data in this group showed longer fixation and visit durations, with EEG showing higher presaccadic potentials on frontal electrodes independent of saccade sizes. Pre-stimulus spectral EEG in the low-alpha (8-10Hz) range showed a tendency towards higher frontal activity, and graph networks demonstrated increased small-world properties with lower frontal degree centrality in the pareidolia group.

Conclusions:: Pareidolias in PD are due to abnormal top-down modulation of visual processing defined by (i) frontal cortex alterations affecting visual attention and guidance to ambiguous stimuli and (ii) network alterations in the pre-stimulus phase due to a dissonance between patients’ internally generated mental-processing with external stimuli.
COMPLETE REMISSION OF SYMPTOMS IN A CASE OF LANCE-ADAMS SYNDROME: A 17-YEAR FOLLOW-UP

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Background and Aims:: Objective: To describe a case of Lance-Adams syndrome in a Movement Disorder Clinic in El Salvador. Background: Chronic post-hypoxic myoclonus, also known as Lance-Adams syndrome, is a rare complication of successful cardiopulmonary resuscitation.

Methods:: We report a case of Lance-Adams Syndrome followed for 17 years with periodic clinical evaluations, video recordings, Barthel Index scale and response to treatment.

Results:: A 50-year-old woman presented with acute intoxication by inhalation of carbamate, followed by bronchospasm, generalized seizures and cardiorespiratory arrest. Brain MRI and EEG were normal. Upon regaining consciousness, she presented spontaneous, action and reflex myoclonus and negative myoclonus, with significant impairment on her activities of daily living and mild cognitive impairment. She presented progressive clinical improvement in response to treatment with valproic acid, phenobarbital and clonazepam. After 4 years of treatment, cognitive impairment and movement disorder resolved, followed by a slow taper of all medications without reoccurrence of symptoms.

Table 1. Clinical evolution and response to treatment over 17 years of patient with Lance-Adams Syndrome

<table>
<thead>
<tr>
<th>CLINICAL FEATURES/YEAR</th>
<th>2004 Pre-Treatment</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008-2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generalized seizures</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Generalized myoclonus:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>· Reflex myoclonus</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>· Action myoclonus</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>· Spontaneous myoclonus</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>· Myoclonic tremor</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>· Gait disorder</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>TREATMENT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>· Valproic Acid</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>· Phenobarbital</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>· Clonazepam</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Gradual taper</td>
<td>-</td>
<td>No</td>
<td>No</td>
<td>yes</td>
<td>yes</td>
<td>Off drugs</td>
</tr>
<tr>
<td>Barthel Index</td>
<td>35/100</td>
<td>55/100</td>
<td>85/100</td>
<td>100/100</td>
<td>100/100</td>
<td>100/100</td>
</tr>
<tr>
<td>MCI present</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>Asymptomatic</td>
</tr>
</tbody>
</table>

MCI: Mild Cognitive Impairment

Conclusions:: We report a case of Lance-Adams syndrome with complete remission of her symptoms after 4 years of treatment and has remained asymptomatic for 13 years after tapering off of medications to control myoclonic activity.
DOES NON-MOTOR PHENOTYPE OF ‘FREEZERS’ DIFFER FROM ‘NON-FREEZERS’ IN PARKINSON’S DISEASE? – A CROSS-SECTIONAL COMPARATIVE STUDY

Ashish Susvirkar
DIVINE LIFE HOSPITAL, KUTCH, Neurology, MUMBAI, India

Background and Aims:: Parkinson disease (PD) is a multi-system disorder having motor and often disabling non-motor manifestations. Pathophysiology of freezing of gait (FOG) seems to be extending beyond motor circuits, into sensory, cognitive and affective neuronal circuits; and, involvement of both dopaminergic and non-dopaminergic mechanisms underlying nonmotor symptoms seem to be involved in FOG also. Aim: To compare the difference in non-motor symptoms between PD patients with freezing of gait (freezers) & those without freezing of gait (non-freezers) matched for age, disease duration, levodopa equivalent doses (LEDD).

Methods:: a) PD-FOG group/ Freezers: Consecutive patients with clinically diagnosed PD (n= 50) using the standard diagnostic criteria (United Kingdom Parkinson’s disease Brain Bank Diagnostic Criteria- Hughes et al 1992) having FOG (diagnosed as per FOG Questionnaire)

b) PD- Non-freezers: PD Patients without FOG who are matched for age, disease duration and LEDD dosage with the PD-FOG group (n= 50). The assessment was done using UPDRS, Hoehn – Yahr scale and Non-motor symptoms assessment using Non-motor symptoms scale (NMSS).

Results::
The freezers group showed statistically significant higher score in domain 2, 3 and 9 which represent sleep/fatigue, mood/cognition, and miscellaneous entities (pain, taste, smell, weight change, excess sweating) respectively, and the total score. Freezers also had statistically significant higher depression scores (BDI).

**Conclusions:** There exists a different nonmotor phenotype in PD patients with FOG with higher nonmotor involvement.

<table>
<thead>
<tr>
<th>Clinical characteristics: Non-motor symptom scale (NMSS) domains</th>
<th>FOG N=50</th>
<th>NON-FOG N=50</th>
<th>p value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1 (Cardiovascular including falls) Median (IQR)</td>
<td>0 (0,1)</td>
<td>0 (0,1)</td>
<td>0.6</td>
</tr>
<tr>
<td>D2 (Sleep/fatigue) Median (IQR)</td>
<td>6.5 (3.75,12.25)</td>
<td>4 (1.75,9)</td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td>D3 (Mood/cognition) Median (IQR)</td>
<td>4 (1, 12.25)</td>
<td>0.5 (0,4.25)</td>
<td><strong>0.001</strong></td>
</tr>
<tr>
<td>D4 (Perceptual problems/hallucination) Median (IQR)</td>
<td>0 (0,1)</td>
<td>0 (0,0)</td>
<td>0.2</td>
</tr>
<tr>
<td>D5 (Attention/memory) Median (IQR)</td>
<td>2 (0,6.25)</td>
<td>1 (0.75,4)</td>
<td>0.5</td>
</tr>
<tr>
<td>D6 (Gastrointestinal tract) Median (IQR)</td>
<td>1 (0,11)</td>
<td>0 (0,2)</td>
<td>0.1</td>
</tr>
<tr>
<td>D7 (Urinary) Median (IQR)</td>
<td>4.5 (1.75,15.25)</td>
<td>2 (0,12)</td>
<td>0.1</td>
</tr>
<tr>
<td>D8 (Sexual dysfunction) Median (IQR)</td>
<td>0 (0,2.5)</td>
<td>0 (0,1)</td>
<td>0.6</td>
</tr>
<tr>
<td>D9 (Miscellaneous) Median (IQR)</td>
<td>6 (1,12)</td>
<td>2 (0,7)</td>
<td><strong>0.01</strong></td>
</tr>
<tr>
<td>Total domain score Median (IQR)</td>
<td>36.5 (17.70)</td>
<td>27.5 (12.7,43.2)</td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td>Montreal Cognitive Assessment (mean ± SD)</td>
<td>26.3 ± 3.44</td>
<td>26.06 ± 2</td>
<td>0.6</td>
</tr>
<tr>
<td>Beck’s Depression Inventory (mean ± SD)</td>
<td>12.18 ± 9.55</td>
<td>7.72 ± 5.76</td>
<td><strong>0.006</strong></td>
</tr>
</tbody>
</table>
It can be further studied as a biomarker and may also open a scope for treatment options of NMS which may affect the development and the course of freezing.
THE REGULATORY EFFECT OF WUZI YANZONG PILL ON UPR SIGNALING PATHWAY IN PARKINSON'S DISEASE MICE

Zhi Chai¹, Hui Jie Fan¹, Yan Rong Li¹, Meng Ying Sun¹, Wu Shuai Xiao¹, Wei Hang¹, Jian Jun Huang², Jie Zhong Yu³, Bao Guo Xiao⁴, Cun Gen Ma¹,³

¹Shanxi University of Chinese Medicine, He Key Research Laboratory Of Benefiting Qi For Acting Blood Circulation Method To Treat Multiple Sclerosis Of State Administration Of Traditional Chinese Medicine And Scientific And Technological Innovation Team Of Integrated Chinese And Western, Jinzhong, China, ²General Hospital of Datong Coalmine Group, General Hospital Of Datong Coalmine Group, Da Tong, China, ³Shanxi Datong University, Institute Of Brain Science- Shanxi Key Laboratory Of Inflammatory Neurodegenerative Diseases, Da Tong, China, ⁴Fudan University, Institute Of Neurology-huashan Hospital-institutes Of Brain Science And State Key Laboratory Of Medical Neurobiology, Shanghai, China

Background and Aims:: Wuzi Yanzong Pill(WYP) has a potential therapeutic effect on Parkinson's Disease(PD) Mice, but the mechanism is not clear. To explore the therapeutic effect of WYP on PD mice and its regulation mechanism on UPR signaling pathway.

Methods:: PD mice were randomly divided into Normal, PD and WYP groups. WYP group were orally administrated with WYP for two weeks and the PD group were treated with same dosage of saline at the same time. Gait test were used to evaluate the behavioral performance. The positive expression of TH was detected by Immunohistochemical staining. The levels of GRP78, p-IRE1α, XBP1, p-PERK, p-eIF2α and ATF4 in brain were detected by Western Blot.

Results:: The results showed that WYP treatment increased the left forelimb angle and findlimb stride length(P<0.05), decreased the total paw area and hindlimb stance width(P<0.05), accompanied by the improvement of TH positive cells(P<0.01). Further observation found that WYP treatment reduced the expressions of GRP78, XBP1, p-PERK, p-eIF2α(P<0.01), ATF4 and p-IRE1α(P<0.05).

Conclusions:: Oral treatment with WYP can alleviate the behavioral and pathological changes in PD mice. Its mechanism may be related to the regulation of IRE1 and PERK signaling pathways.(Grants: NNSF of China 81102552 and 81703978, Central Government Guided Local Funding Projects for Science and Technology Development YDZX2020140001483, Returned Chinese Scholars Technology Activities Preferred Project, Shanxi Province of China 202000026, Natural Science Foundation of Shanxi Province 201901D111334, Key Research and Development Projects of Shanxi Province 201803D31209, Shanxi University Science and Technology Innovation Project 2019L0724.*corresponding authors: Prof. C.G. Ma or Prof. H.J. Fan.)
WUZI YANZONG PILL, A CLASSICAL HERBAL FORMULA, EXHIBITS THERAPEUTIC POTENTIAL IN TREATING PARKINSON’S DISEASE

Hui Jie Fan1, Zhi Chai1, Yan Rong Li1, Meng Ying Sun1, Wu Shuai Xiao1, Jian Jun Huang2, J.Z. Yu3, Bao Guo Xiao4, Cun Gen Ma1,3

1Shanxi University of Chinese Medicine, The Key Research Laboratory Of Benefiting Qi For Acting Blood Circulation Method To Treat Multiple Sclerosis Of State Administration Of Traditional Chinese Medicine And Scientific And Technological Innovation Team Of Integrated Chinese And Western, Jinzhong, China, 2General Hospital of Datong Coalmine Group, General Hospital Of Datong Coalmine Group, Datong, China, 3Shanxi Datong University, Institute Of Brain Science- Shanxi Key Laboratory Of Inflammatory Neurodegenerative Diseases, Datong, China, 4Fudan University, Institute Of Neurology-huashan Hospital-institutes Of Brain Science And State Key Laboratory Of Medical Neurobiology, Shanghai, China

Background and Aims:: Wuzi Yanzong Pill(WYP) has a potential therapeutic effect on Parkinson’s Disease(PD) mice, but the effect to ERS-mediated apoptosis pathway in PD were not studied. To determine the therapeutic effect of WYP on PD mice and explore its mechanism.

Methods:: C57BL/6 mice were randomly divided into normal control, PD control, and WYP groups. The WYP group was orally administrated with WYP for 14 days while the normal and PD groups were treated with saline. The ethology were detected by open field and pole tests. The positive expression of TH was detected by Immunohistochemical method. Western Blot were used to detect the contents of Caspase-9, CHOP, ASK1, p-JNK, Caspase-3 and Caspase-12.

Results:: Compared with the model group, WYP reduced the pole climbing and total resting time(P<0.05), enhanced the total distant(P<0.01) and mean speed(P<0.05). TH+ neuron in substantia nigra increased after WYP treatment(P<0.05), while the levels of CHOP(P<0.01), Caspase-9 and Caspase-12 decreased(P<0.05). There was no statistically significant change in protein content of ASK1, p-JNK and Caspase-3 in all the three groups.

Conclusions:: WYP can improve the balance and coordination ability and alleviate the pathological changes in PD mice. Its mechanism may be related to inhibit the CHOP and Caspase-12 apoptosis pathways.(Grants: NNSF of China 81102552 and 81703978,Central Government Guided Local Funding Projects for Science and Technology Development YDZX20201400001483, Returned Chinese Scholars Technology Activities Preferred Project, Shanxi Province of China 20200026,Natural Science Foundation of Shanxi Province 201901D111334,Key Research and Development (R&D) Projects of Shanxi Province 201803D31209,Shanxi University Science and Technology Innovation Project 2019L0724.*corresponding authors: Prof. C.G. Ma or Prof. Z.Chai)
THE MECHANISM OF WUZI YANZONG PILL IN THE PREVENTION AND TREATMENT OF PARKINSON'S DISEASE BASED ON PI3K-AKT SIGNALING PATHWAYS

Zhi Chai¹, Hui Jie Fan¹, Wei Hang¹, Yan Rong Li¹, Meng Ying Sun¹, Li Juan Song¹, Lu Jia¹, Jian Jun Huang², Jie Zhong Yu³, Bao Guo Xiao⁴, Cun Gen Ma¹,³

¹Shanxi University of Chinese Medicine, The Key Research Laboratory Of Benefiting Qi For Acting Blood Circulation Method To Treat Multiple Sclerosis Of State Administration Of Traditional Chinese Medicine-And Scientific And Technological Innovation Team Of Integrated Chinese And Western, Jinzhong, China, ²General Hospital of Datong Coalmine Group, General Hospital Of Datong Coalmine Group, Da Tong, China, ³Shanxi Datong University, Institute Of Brain Science- Shanxi Key Laboratory Of Inflammatory Neurodegenerative Diseases, Da Tong, China, ⁴Fudan University, Institute Of Neurology-huashan Hospital-institutes Of Brain Science And State Key Laboratory Of Medical Neurobiology, Shanghai, China

Background and Aims:: Network pharmacology is a biological network analysis method that combines systems biology, pharmacology and computer technology To explore the prevention and treatment of Wuzi Yanzong Pill(WYP) on Parkinson's Disease(PD) mice based on the PI3K/Akt signaling pathways.

Methods:: Network pharmacology was used to screen the potential signaling pathways of WYP in treating PD. PD model was established by MPTP. At the same time, oral administration of WYP was carried out twice a day for 14 consecutive days. Mice motor function was evaluated by Pole test. Expression of dopamine in brain tissue were detected by ELISA. The expression levels of tyrosine hydroxylase(TH) was determined by immunofluorescence analysis. Expression of PI3K, p-PI3K, Akt and p-Akt were determined by Western Blot.

Results:: The results of network pharmacology identified 125 candidate targets, and pathways analysis showed that the treatment mechanism for PD mainly involved HIF-1, PI3K/Akt signaling pathways, dopaminergic synaptic and insulin resistance pathways and so on. Behavioral test showed that the motor performance of mice was improved after WYP treatment. WYP enhanced the number of TH neurons and expression of dopamine (P<0.05). The expressions of p-PI3K and p-Akt were increased after WYP administration (P<0.05) in PD model.

Conclusions:: Maybe WYP protect dopamine neurons from loss in the MPTP mice model of PD through activation of PI3K/Akt signaling pathways.(Grants: NNSF of China 81102552 and 81703978, Central Government Guided Local Funding Projects for Science and Technology Development YDZX20201400001483, Natural Science Foundation of Shanxi Province 201901D111334, Shanxi University Science and Technology Innovation Project 2019L0724.*corresponding authors: Prof. C.G. Ma or Prof. H.J. Fan)
CLINICO-GENETIC PROFILE AND TREATMENT OUTCOMES OF INHERITED HYPERMANGANESEMIA AMONG INDIAN CHILDREN: A MULTICENTRIC STUDY

Divyani Garg1, Sangeetha Yoganathan2, Arushi Saini3, Naveen Sankhyan3, Umesh Kalane4, Kavita Srivastava5, Abhijeet Botre6, Debasis Panigrahi7, Hansashree Padmanabha8, Mahesh Kamate9, Monica Juneja10, Vrajesh Udani11, Suvasini Sharma12

1Lady Hardinge Medical College, New Delhi-110001, Neurology, New Delhi, India, 2Christian Medical College, Neurology, Vellore, India, 3Post Graduate Institute of Medical Education and Research, Pediatrics, Chandigarh, India, 4Deenanath Mangeshkar Hospital and Research Center, Pediatric Neurology, Pune, India, 5Bharati Vidyapeeth Medical College, Pediatrics, Pune, India, 6KEM Hospital, Pediatrics, Pune, India, 7Jagannath Hospital, Pediatrics, Bhubaneswar, India, 8NIMHANS, Neurology, Bangalore, India, 9JN Medical College, Pediatrics, Belgaum, India, 10Maulana Azad Medical College, Pediatrics, Delhi, India, 11PD Hinduja Hospital, Pediatrics, Mumbai, India, 12Lady Hardinge Medical College, Pediatrics (neurology Division), New Delhi, India

Background and Aims:: Inherited hypermanganesemia (IH-Mn) is a rare inherited manganese (Mn) transport defect, characterized by two phenotypes due to mutations in SLC30A10 and SLC39A14 genes. We aimed to describe clinical, laboratory and genetic profile of children with IH-Mn.

Methods:: We conducted a multicentric retrospective study across 11 centers in India. We collected data pertaining to clinical, laboratory profile and treatment outcomes among children between 1 month-18 years of age with genetically confirmed/ clinically probable IH.

Results:: We enrolled 27 children from 20 families (19 girls). Fourteen harbored SLC39A14 mutations; nine had SLC39A14 mutations. The SLC39A14 cohort had lower median age at onset [1.3 (IQR 0.7-5.5) years] versus SLC30A10 cohort [2.9 (IQR 1.6-4.5) years]. The most frequent neurological features were dystonia (100%), gait abnormality (80.8%; n=21), falls (69.2%; n=18) and parkinsonism (61.5%; n=16). Median blood Mn levels among SLC39A14 [101.8 (IQR 28.5-200.0) mcg/L] were higher than SLC30A10 cohort [34.0 (23.9-100.0) mcg/L]. Median hemoglobin was higher in SLC30A10 [16.1 (IQR 15.2-17.5) g/dL] versus SLC39A14 cohort [11.7 (IQR 8.8-13.2) g/dL]. The SLC39A14 cohort had more severe disease evidenced by more frequent generalized dystonia, dependent ambulation and blood Mn. All children underwent chelation with disodium-calcium edetate. Children with SLC39A14 mutations had poorer response, scored on a Likert scale. Nine children were lost to follow-up.

Conclusions:: We describe the largest pediatric cohort of IH till date. Children with SLC39A14 mutations were younger, had more severe disease and poorer treatment response versus SLC30A10 mutations. There is emerging need to better define management strategies for these children.
PREFRONTAL ACTIVITY IMBALANCE AND ABERRANT RECONFIGURATION ACROSS FUNCTIONAL NETWORKS IN PATIENTS WITH PARKINSON’S DISEASE AND SOMATIC SYMPTOM DISORDER

Stefano Delli Pizzi, Raffaella Franciotti, Piero Chiacchiaretta, Antonio Ferretti, Astrid Thomas, Laura Bonanni, Stefano Sensi, Marco Onofrj
Università “G. d’Annunzio” di Chieti-Pescara, Department Of Neuroscience, Imaging And Clinical Science, Chieti, Italy

Background and Aims:: The altered activity and neurotransmission of the medial prefrontal cortex (mPFC), a key node of the default-mode network, has been associated with the presence of somatic symptom disorder (SSD), a highly prevalent neuropsychiatric disorders in Parkinson's disease (PD). We investigated whether, in SSD patients, the altered activity of the mPFC promotes a functional reconfiguration across brain networks and whether these changes are specific hallmarks of the presence of SSD in PD.

Methods:: A multimodal magnetic resonance imaging (MRI) protocol assessed the neurochemistry and functioning of the mPFC in a cohort of sixty-six individuals. The study cohort included seventeen PD patients with SSD, eighteen PD patients, twelve SSD patients unaffected by any neurological or other psychiatric condition, and nineteen healthy control (HC) subjects.

Results:: Compared to HC or PD individuals, PD+SSD and SSD patients exhibited altered prefrontal activity. They also showed increased functional connectivity between the mPFC and critical nodes of the fronto-parietal control network. While SSD patients’ enhanced connectivity was limited to the lateral prefrontal cortex, the distinct functional reorganization of PD+SSD patients also included posterior brain regions. Compared to HC subjects, PD+SSD patients, but not SSD patients, exhibited an anterior-to-posterior shift of resting-state brain activity that involved the same areas that showed increased connectivity.

Conclusions:: Our findings identify a pathophysiologic role of the dysfunctional activity of the mPFC. The data indicate an aberrant reconfiguration across DMN and Cont, a potential functional SSD signature in patients with PD.
GAIT AND TURNING ALTERATIONS IN IDIOPATHIC REM SLEEP BEHAVIORAL DISORDER AND EARLY PARKINSON’S DISEASE: A CROSS-SECTIONAL STUDY WITH MOBILE HEALTH TECHNOLOGY.

Marcello Catania¹, Andrea Pilotto¹, Andrea Galbiati², Clint Hansen³, Rob Romijnders³, Andrea Corbani¹, Sara Nocivelli¹, Stefano Masciocchi⁴, Alberto Imarisio¹, Maria Rizzetti⁵, Luigi Ferini-Strambi², Walter Maetzler⁶, Alessandro Padovani⁷

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Background and Aims:: Subtle motor impairment and slowness of movements are early features of Parkinson’s disease and might be present already in the prodromal phase. Subjects with idiopathic REM sleep behavior disorder (RBD) are at high risk of developing PD.

Methods:: The aim of the study was investigate the differences in performances of gait and turning under supervised conditions in healthy controls, idiopathic REM sleep behavior disorder (RBD) and patients with Parkinson’s disease. Each participant underwent a supervised mobile health technology-instrumented assessment including the timed up and go test and one minute walking tasks with turns in normal and dual task conditions (cognitive task, motor task).

Results:: Results Sixty-eight PD patients (26 drug naïve and 42 under treatment, mean UPDRS-III 15±9), 18 RBD (mean UPDRS-III 1±1) and 33 age-matched controls entered the study. Compared to controls, PD patients (both naïve and under treatment) needed more time to perform the TUG. During straight walking, the showed higher stride time, higher double limb support variability and a higher asymmetry index. Moreover, they turned slower than controls. Compared to controls, RBD subjects showed a higher swing time and turned slower.

Conclusions:: Discussion This study suggests that RBD patients have a gait pattern that is distinguishable from controls and show features comparable to early PD patients. These results partly support results from a recent study investigating RBD gait in free-living conditions (Del Din et al, JPD, 2020), and build a bridge between the control and PD state. Future studies using mobile health technology are needed to evaluate the predictive capacity of the method, to define RBD subjects that are in prodromal PD phases.
ASSOCIATION BETWEEN SLEEP DISORDERS AND COGNITIVE DYSFUNCTIONS IN ADVANCED PARKINSON’S DISEASE

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\textbf{Background and Aims::} Parkinson’s disease (PD) is increasingly recognized as a multidimensional disorder, characterized by several non-motor symptoms, including cognitive and sleep disturbances. Our aim is to explore associations between subjectively reported sleep alterations and cognitive functions in advanced PD.

\textbf{Methods::} 181 advanced PD patients completed two self-administered sleep measures: the PD Sleep Scale (PDSS-2) and the Epworth Sleepiness Scale (ESS). Neuropsychological assessment encompassed five cognitive domains: reasoning [Raven Coloured Progressive Matrices Test (RCPMT)]; memory [Corsi’s Block Tapping Test (CBT), Paired Associate Learning (PAL)]; attention [Digit Cancellation Test (DCT), Trail Making Test A (TMT-A)]; frontal executive functions [Trail Making Test B (TMT-B), Frontal Assessment Battery (FAB)]; language [phonemic and semantic verbal fluency (PVF, SVF)].

\textbf{Results::} Patients showed mild to moderate sleep problems (PDSS-2: 23.4±1.2) and mild daytime sleepiness (ESS: 8.6±5.1). A significant correlation was observed between higher PDSS-2 scores, indicative of greater sleep disturbances and measures of reasoning (RCPMT: $\beta=-0.214$; $p=0.002$), attention (DCT: $\beta=-0.194$; $p=0.007$), executive functions (FAB: $\beta=-0.139$; $p=0.049$; TMT-B: $\beta=0.156$; $p=0.031$) and category verbal fluency (CVF: $\beta=-0.167$; $p=0.027$). No significant correlations were found between PDSS-2 scores and memory test scores, nor between ESS score and any of the neuropsychological tests.

\textbf{Conclusions::} Our study shows that in advanced PD, sleep disturbances selectively correlate with subcortical neuropsychological functions and not with short-term memory and consolidation. Further studies are needed to determine whether sleep disorders are risk factors for cognitive decline and dementia in PD, and to understand the underlying mechanisms.
RECENT ADVANCES IN THE SEARCH OF SPECIFIC BIOMARKERS FOR SYNUCLEINOPATHIES

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Background and Aims:: Synucleinopathies are neurodegenerative disorders characterized by the abnormal deposition of misfolded α-synuclein (α-syn) mainly in neurons. They include common disorders such as Parkinson disease or Dementia with Lewy bodies. The premortem diagnosis of synucleinopathies lacks a specific biomarker and their diagnosis is mainly based on clinical criteria, leading to frequent misdiagnosis. The search of easily applicable diagnostic test with high sensitivity and specificity is not currently available for synucleinopathies in the clinical practice although urgently needed. This review gives an overview on the sensitivity and specificity of new diagnostic tools to identify in vivo pathological α-syn.

Methods:: We analysed papers reporting new diagnostic tools aimed at disclosing in vivo misfolded α-syn. We focused our analysis on diagnostic accuracy and practicability in the clinical routine work. Furthermore, our analysis addresses methodological problems and the lack of standardized procedures of these techniques. Finally, we give an outlook on the future of these techniques as a potential diagnostic tool

Results:: In the recent years two promising tools have been settle up to identify in vivo misfolded α-synuclein: immunofluorescence (IF) and RT-QuIC. They both show a high diagnostic accuracy in differentiating patients with synucleinopathies from different neurodegenerative and other neurological disorders and present an excellent practicability in the clinical work. However IF displayed an optimal level of reproducibility which needs to be established for RT-QuIC

Conclusions:: Emerging techniques as immunofluorescence (IF) and RT-QuIC show promising diagnostic accuracy and practicability for the in vivo diagnosis of synucleinopathies although some aspects need to be improved to increase their clinical application
Background and Aims:: BACKGROUND/AIMS: Statins are speculated to be neuroprotective and are associated with the reduced risk of Parkinson’s disease (PD) but only a few studies have investigated the influence of statins on PD progression. To evaluate whether long-term statin use may affect motor progression in a large cohort of de novo patients with PD.

Methods:: METHODS: We conducted a 4-year retrospective observational cohort study assessing patients with PD who were consecutively recruited from a single tertiary center between January 2015 and January 2017. Information on motor function was obtained using the MDS-Unified Parkinson Disease Rating Scale (UPDRS)-III and all subjects were extensively characterized, including about lifestyle habits, cardiovascular risk factors and cholesterol blood levels.

Results:: RESULTS: Of the 181 participants included in the study, 104 patients were evaluated for eligibility (42 patients were exposed to statin therapies and 62 were not treated with statins). Patients presented similar scores in UPDRS III at baseline but statin users had a lower motor impairment at 4 years compared to non-users PD patients. Additionally, statin treatment resulted in less progression of rigidity score of UPDRS over 4 years. No other significant differences were observed between PD patients with and without statins.

Conclusions:: CONCLUSIONS: Early PD patients with long-term statin usage showed lower motor deterioration after 4 years of disease duration compared with patients not taking statins at diagnosis, suggesting a possible influence of statins on disease progression in PD. Further investigation is warranted in order to understand the potential beneficial effects of statin treatment on clinical symptoms in PD.
INTRODUCTION TO THE TOPIC:

Intrinsically Functional Connectivity Changes in Drug-Naïve Parkinson’s Disease Patients with Mild Cognitive Impairment

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Background and Aims:: Mild cognitive impairment (MCI) is a common nonmotor symptom in Parkinson’s disease (PD) and it is considered a risk factor for developing dementia. Using resting-state functional MRI, we investigated intrinsic brain networks connectivity correlates of MCI in a cohort of drug-naïve patients with PD.

Methods:: 3T MRI images of 40 drug-naïve non-depressed PD patients (PD-MCI and PD-noMCI), and 20 matched healthy controls (HCs) were analyzed. MDS Task Force Level II diagnostic criteria were applied to determine the presence of MCI. Single-subject and group-level independent component analysis was used to investigate intra and inter-network functional connectivity differences within the major neurocognitive networks between patients subgroups and HCs. Linear regression analysis was used to investigate correlations between imaging and clinical data.

Results:: Compared to PD-noMCI patients, PD-MCI patients showed decreased connectivity within the right frontoparietal, the default-mode and the ventral attention networks. Inter-network connectivity between default-mode/dorsal attention and default-mode/ventral attention networks were significantly positive in PD-MCI patients compared to PD-noMCI. Functional connectivity changes within and between neurocognitive networks were found to be correlated with neuropsychological outcomes.

Conclusions:: Our findings demonstrate the presence of specific intrinsic functional connectivity changes involving the most important neurocognitive networks in early PD patients with MCI. This connectivity pattern is not biased from dopaminergic medication and it is also correlated with symptoms severity. We hypothesize that this functional architecture may reflect the presence of diffuse neuropathological changes, which may represent a potential early biomarker for developing clinically significant cognitive impairment over time.
Background and Aims:: Vascular Parkinsonism (VP) is a type of Parkinson's disease (PD), the course, treatment, and origin of these two diseases are radically different.

Methods:: To compare the first signs of the disease, clinical-anamnestic, neurological examination and retrospective analysis of 47 patients with PD and 40 patients with VP hospitalized at the TMA were carried out, and a special questionnaire was compiled.

Results::

<table>
<thead>
<tr>
<th>Gender and age</th>
<th>PD (n=47)</th>
<th>VP (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>28 (59.4%)</td>
<td>27 (67.5%)</td>
</tr>
<tr>
<td>Women</td>
<td>19 (40.5%)</td>
<td>13 (32.5%)</td>
</tr>
<tr>
<td>The mean age</td>
<td>52.4±4.3</td>
<td>61.3±4.4</td>
</tr>
<tr>
<td>The mean age of onset of the disease</td>
<td>50.9±2.3</td>
<td>58.4±4.3</td>
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</table>

When the origin of VP was studied in patients, 27.5% of patients developed VP after stroke, 40% developed on the background of diabetes mellitus, 72.5% of patients developed VP on the background of chronic cerebral ischemia, 22.5% of patients had a history of myocardial infarction in diabetic patients. These results confirm that diabetes mellitus, chronic cerebral ischemia, strokes, and myocardial infarction are among the factors contributing to the development of VP. In 40% of cases, the first symptoms of the disease began with slowing of movement, only in 9% of cases the first sign of the disease began with tremors. In PD, the first sign of the disease was tremors, in 86% of patients was unilateral onset, in 72% of patients tremors only in the hands, and in 42% only in foot. In VP, the disease was observed symmetrically in 68% of cases and began mainly in the foot.

Conclusions:: Although both VP and PD are associated with movement disorders, the diagnosis and treatment of this disease require a different approach due to the fact that they are radically different.
NEUROPROTECTIVE EFFECT OF HYPEROSIDE ON MPTP/MPP+-INDUCED PD MODEL

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Background and Aims:: Hyperoxide (HYP), the natural active component of Wuzi Yanzong Pill, showed a therapeutic potential on Parkinson's disease (PD) mice. To explore the therapeutic effects and its possible mechanisms of HYP on PD mice.

Methods:: SH-SY5Y cells were incubated with MPP⁺ for 24 h with or without HYP treatment, followed by a detection of cell viability and mitochondrial membrane potential. The male C57BL/6 mice were randomly divided into three groups: normal, MPTP and HYP group. PD model was induced by intraperitoneal administration of MPTP for 7 days and simultaneously received intraperitoneal injection of HYP for 7 or 14 days, followed by a detection of gait test and pathology alternations by immunofluorescence and western blot. In mice brain homogenate and cell supernatant, inflammation factors and oxidative stress were measured by ELISA, respectively.

Results:: HYP treatment declined the apoptosis of SY5Y cells under MPP⁺ injury. Compared with the PD mice, HYP treatment significantly improve the motor dysfunction of PD mic after 7 or 14 day and increased the number of TH⁺ neuron. Meanwhile, HYP treatment significantly increased the expression of p-AKT in SY5Y cells and GFAP⁺ or Iba1⁺ cells. HYP treatment also significantly decreased in the expression of inflammatory factors (IL-6, IL-1β and TNF-α) and the level of MDA and GSH both in vitro and in vivo.

Conclusions:: These results revealed the neuroprotective of HYP for PD through anti-inflammation and antioxidation via enhancing the phosphorylation of AKT.(Grants: NNSF of China 81102552 and 81703978,Central Government Guided Local Funding Projects for Science and Technology Development No. YDZX20201400001483.*corresponding authors: Prof. C.G. Ma or Prof. H.J. Fan)
FINGERPRINT OF GAIT APPLIED TO PARKINSON’S DISEASE

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Background and Aims:: Many Neurological diseases provoke motor impairment. In order to obtain early diagnosis and effective assessment of therapeutic outcomes, it is desirable to quantify gait features and alterations. In this study, we showed that human gait is characterized by replicable patterns of consensual accelerations/decelerations of body segments, that are highly regulated. Hence, we analysed motion analysis data through a graph theoretical approach and applied this framework in Parkinson’s disease (PD), showing the utility of our newly proposed technique in clinical settings.

Methods:: We recruited twenty-three PD patients, off medication, and twenty-tree healthy subjects (HS). Both groups underwent gait analysis through a stereophotogrammetric system acquiring the instantaneous position of 21 anatomical markers and computed their velocity, acceleration, and jerk. We correlated the time series among the markers, obtaining an adjacency matrix of the consensual movements of the body segments, that we named “kinectome”. Beyond a fingerprint analysis we performed a topological analysis considering the markers as nodes, and the correlation coefficients between markers as edges.

Results:: The PD group kinectomes showed higher standard deviation values compared to HS, showing that the gait patterns are steadier in the healthy. Consequently, while kinectomes allow the identification of each individual, PD showed lower identifiability as the motor impairment increases. Topological analysis revealed a reduction of the centrality of the markers corresponding to the upper limbs proportional to the reduction of stability of gait.
HS group

PD group
Conclusions: Network analyses of human movement through kinectome is a novel technique for movement analysis and is able capture and characterize motor impairment in PD.
**FOLLOW-UP EVALUATION OF MOTOR AND NON-MOTOR SYMPTOMS IN ESSENTIAL TREMOR**

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**Background and Aims::** Essential Tremor (ET) is a common and heterogeneous movement disorder characterized by action tremor of upper limbs and other body parts, as well as non-motor symptoms (e.g., cognitive and psychiatric abnormalities). However, only few studies have attempted to estimate symptoms progression in ET.

**Methods::** We enrolled 18 patients with ET. Each patient underwent the same evaluation at baseline and during a follow-up assessment (mean follow-up interval: 33.5 months; range: 21 – 45 months). We assessed tremor by mean of clinical rating scales and kinematic recordings; patients also underwent neuropsychological tests for cognitive assessment and structured interviews to investigate psychiatric disorders.

**Results::** At follow-up evaluation we observed higher Tremor Rating Scale scores than baseline (31.1±13.3 vs. 20.9±10; $P<0.05$) reflecting the involvement of more than one body segment e.g., upper limb plus head, voice, tongue, and lower limbs (baseline: 38.9% vs. follow-up: 77.8%; $P<0.05$). Kinematic analyses, however, did not reveal amplitude and frequency changes of head or upper limb tremor over time (all $P_s<0.05$). Also rest tremor was less frequent at baseline compared to follow-up (33.3% vs. 77.8%; $P<0.05$). Cognitive assessment showed cognitive worsening in 6 out of 18 cases (33.3%). Finally, psychiatric assessment showed a trend toward reduction in anxiety and depression over time.

**Conclusions::** ET is a progressive disorder with tremor spread in multiple body segments over time and emergence of soft signs, e.g., rest tremor and cognitive abnormalities. Further observations are needed to identify possible predictors in the rate of progression of motor and non-motor domains.
FREEZING OF GAIT IN SUBTHALAMIC DEEP BRAIN STIMULATION FOR PARKINSON DISEASE: A PILOT STUDY ON SAFETY AND TOLERABILITY OF VARIABLE VERSUS LOW FREQUENCIES STIMULATION

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Background and Aims:: Background and aims: Low frequency (LS) subthalamic deep brain stimulation (STN-DBS) may have a benefit on Parkinson’s disease (PD) axial sings, especially on freezing of gait (FOG). However, this benefit seems to not be maintained over time. Phenomena of neuronal adaptation could be related to the development of this tolerance. The aim of this study is to verify the safety and tolerability of variable frequency (VF) versus LFS among PD patients with severe FOG.

Methods:: a randomized-double blind pilot study on PD patients with STN-DBS with severe FOG underwent one month of LFS during 24h/day and one month of VFS (LF during 16 h/daytime and high frequency stimulation [HFS] during 8h night-time) in a randomized fashion. Motor and cognitive outcome were assessed at each timepoint.

Results:: we recruited 10 patients with a median age and disease duration of 66 [IQR: 62-71] and 17.5 [IRQ: 13.5 – 21.2] years. Two patients were excluded, three patients dropped out after one week of VFS. Among the five remaining patients, comparing both LFS and VFS with HFS, we found a not statistically significant improvement of FOG. No statistically cognitive changes were found, and no adverse event occurred with both stimulation parameters.

Conclusions:: VFS seems to be as effective as safe as LFS among patients with severe FOG, offering a benefit on axial signs. The small sample of recruited patients of our pilot study did not allow to reach statistically significant results. Our findings need to be confirmed in a larger cohort of patients.
Background and Aims:: The aim of this study was to analyze the clinical features of benign essential blepharospasm (BEB) in Latvian patients. To our knowledge, this is the first study describing clinical features of BEB patients in Latvia.

Methods:: 56 patients were included in this retrospective analysis. The data were collected from medical records and phone interviews.

Results:: The mean age of the disease onset was 57.5 +/- 11.7 (range, 23-80 years), 77% (n=43) were women. Antagonistic maneuvers were positive in 57% (n=32) of all cases. The most common aggravating factor was bright light (75%, n=42) and watching at screens (38%, n= 21). [Image1]. Only 13% (n=7) denied any aggravating factors. In this study, 50% (n=23) of patients reported stressful event before symptom development, the most common - a death of a relative (40% of those cases, n=9). Non-motor symptoms (psychiatric, sleep disturbances and ocular non-motor symptoms) were positive in 75% (n=42). Almost one third of patients (30%, n=17) had co-existing depression, 20% (n=11) – general anxiety disorder. 46% (n=26) of patients experienced sleep disturbances.

The time from symptom onset till first injection with botulinum toxin type A (BoNT) was 5.5 +/- 7.7 (range, 0-49 years), half of patients received BoNT injection treatment within first three years.

Conclusions:: Whether a coincidence or triggering factor but 50% of patients linked a stressful event with beginning of BEB. In Latvia half of the patients still receive treatment more than 3 years after the onset of symptoms. Non-motor symptoms in BEB is a major component of condition, which are often overlooked.
GLUCOCEREBROSIDASE ACTIVITY AND TRANSPORT TO LYSOSOMES IN PRIMARY MACROPHAGES FROM PATIENTS WITH MUTATIONS IN THE GBA GENE

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Background and Aims:: Mutations in GBA alters glucocerebrosidase (GCase) transport to lysosomes and leads to Gaucher disease (GD) development and also the most important genetic risk factor for Parkinson's disease (PD). However, the majority of GD patients and carriers do not develop PD, suggesting the possibility of other disease modifying factors. To study the glucocerebrosidase (GCase) activity and translocation to lysosomes in primary macrophages derived from PD patients with GBA mutations (GBA-PD) and asymptomatic carriers of GBA mutations (asympGBA).

Methods:: Mononuclear fraction was isolated from whole blood of GBA-PD (N=9), asympGBA (N=12) and healthy controls (N=22). With subsequent differentiated into macrophages using RPMI supplemented with 10% FBS, 1% streptomycin-penicillin and 10 ng/ml M-CSF for 4 days. GCase enzymatic activity was measured by LC-MS/MS in dry macrophage cell spots on filter paper. The translocation of GCase (Alexa Fluor 488) to lysosomes (LAMP2(Cy3)) was demonstrated in primary macrophages using a Leica TCS-SP5 confocal microscope.

Results:: In our study, we showed differences in GCase activity in primary macrophages derived from GBA-PD, asympGBA patients and controls (Table 1).

Table 1. GCase activity in PBMC-derived macrophages.

<table>
<thead>
<tr>
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<th>GCase activity, mmol/l/h (median min – max)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBA-PD (N=9)</td>
<td>12.54 (3.78 – 24.28)</td>
<td>0.983</td>
</tr>
<tr>
<td>Asymp – GBA (N=12)</td>
<td>4.05 (1.15 – 24.16)</td>
<td>0.001 *</td>
</tr>
<tr>
<td>Control (N=22)</td>
<td>12.68 (6.05 – 70.98)</td>
<td>-</td>
</tr>
</tbody>
</table>

* compared to controls

A decreased translocation of GCase to lysosomes by decreased colocalization of GCase with the lysosomal marker LAMP2 was observed in primary macrophages derived from GBA-PD 0.64 (0.48-0.86) and asympGBA 0.63 (0.54-0.688) patients compared to controls 0.76 (0.62-0.86) (p<0.0001, p=0.0001).

Conclusions:: GCase transport to lysosomes is impaired in primary macrophages derived from patients with GBA mutations. Asymptomatic carriers of GBA mutations characterized by decreased GCase activity in primary macrophages. The study was supported by RSF № 19-15-00315.
A POTENTIAL RESCUE STRATEGY IN A CASE OF STN-DBS OFF-TARGETING: THE ANODIC STIMULATION.

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Background and Aims: An off-targeting implantation remarkably interferes with deep brain stimulation outcome, because of the engagement of nearby cerebral structures and therefore side effects. This study aims at evaluating the potential therapeutic opportunities offered by advanced programming for off-targeting DBS.

Methods: A 56 y.o. male was implanted with bilateral STN-DBS with directional leads and an implantable pulse generator able of Multiple Independent Current Control. Low amplitude threshold for left facio-brachial tonic spams was revealed at monopolar review, interfering with the clinical outcome. Reducing the amplitude in monopolar (even directional) stimulation, programming in bipolar or as guarded cathode did not improve the therapeutic window. This prompt us to explore novel programming options, namely low/high frequency, low pulse width and anodic stimulation, after carrying out a post-operative neuroimaging processing.

Results: As suggested by monopolar review, left lead run laterally to the planned target within the medial part of the corticospinal tract at the postprocessing neuroimaging. We found that anodic stimulation decreased the corticospinal tract engagement compared to the cathodic one with further improvement of bradykinesia and rigidity by lowering the pulse width. Moreover, bilateral high frequency resulted in tremor reduction.

Conclusions: This case highlights the potential advantages of anodic stimulation in lateral off-targeting in STN-DBS, lowering the corticospinal tract engagement.
KINEMATIC ASSESSMENT OF BRADYKINESIA DUE TO FOCAL BASAL GANGLIA LESION: A SERIES OF TWO ISCHEMIC STROKE CASES

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Background and Aims:: Focal lesions of the basal ganglia due to stroke can induce various movement disorders, including parkinsonism. To date, there are no objective measurement of bradykinesia features in patients with parkinsonism due to structural lesions of the basal ganglia and it is unknown whether they differ from those observed in parkinsonism of other origins. We here reported two cases of focal ischemic stroke of the basal ganglia and unilateral parkinsonism. Besides the clinical description, we also aimed to characterize the kinematic features bradykinesia in these two patients.

Methods:: Repetitive finger tapping was kinematically recorded using a motion analysis system in one patient with a lesions of the left substantia nigra (case 1) and in one patient with a lesion of the right stratum (case 2). Movement velocity, amplitude, rhythm, and decrement (sequence effect) were measured. Patients' kinematics were compared with those of 65 healthy controls.

Results:: In Case 1, the prominent bradykinesia features were severe movement slowness with sequence effect. In Case 2, we observed severely reduced movement amplitude and to a lesser extent slowness and altered rhythm, but no sequence effect.

Conclusions:: Bradykinesia has heterogeneous features in parkinsonism due to focal brain lesions, depending on the lesion topography, and it may resemble bradykinesia features previously observed in idiopathic Parkinson’s disease and atypical parkinsonism. The results may give insight for a better understanding of bradykinesia pathophysiology and support the hypothesis of bradykinesia as a network disorder, in which the disfunction of specific nodes results in the different features.
A FRAMEWORK ANALYSIS ON DYSTONIC PATIENTS’ EXPERIENCES OF FIRST-WAVE OF COVID-19 PANDEMIC

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Background and Aims:: The first wave of the SARS-CoV2 pandemic imposed healthcare reorganization in order to tackle the infection spread. Prioritizing COVID-19 related management risked leaving rare chronic diseases without proper care response. This study aims at analysing the dystonic patients’ (DPs) experiences during the pandemic.

Methods:: A nation-wide survey consisting of 37 items (demographic, dystonic syndrome and qualitative information) was disseminated online before the second wave spread and DP were anonymously recruited. The data collected were analyzed by descriptive statistics and qualitative framework analysis.

Results:: 62 DPs answered the survey, half of them from the Italian “red-zones”. Pandemic elicited negative emotions in 50% of participants. DPs experienced a rebound of motor and non-motor symptoms with severe repercussion on job and daily functionings. In-person outpatient clinics (including i.e. botulinum neurotoxin injection, physiotherapy session) were shutdown with high rate, where less frequently telephone/mail contacts with the healthcare providers. Despite efforts, DPs felt were not satisfactorily supported.

Conclusions:: During the first wave pandemic, dystonia-related issues were frequently not well-managed with negative consequences on symptoms and DPs’ daily functioning. We hope these findings might raise awareness about DPs’ unmet needs. Comprehending DPs’ perspectives may inform healthcare provision in the next step of this pandemic. Despite efforts, telemedicine might not be leveraged alone for movement disorders management during this pandemic. We acknowledge the support of the Italian Association of the research against Dystonia (Associazione Italiana per la Ricerca sulla Distonia).
GUT MICROBIOTA DYSBIOSIS IN PARKINSON'S DISEASE PATIENTS: EARLY FEATURE AND BIOMARKER OF DISEASE PROGRESSION?

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Background and Aims:: Gut microbiota dysbiosis is considered an hallmark in Parkinson's disease (PD). However, it is still unclear whether microbiota alterations, in PD, represent a pathogenetic starting point or also a consequence of disease. Our aim was to investigate microbiota alterations in PD patients at the time of diagnosis and in later stages of the disease, in order to identify dysbiosis not only as an early non-motor feature but also as a biomarker of disease progression.

Methods:: 108 faecal samples were collected from 30 PD patients at the time of diagnosis (de novo PD), 38 PD patients in advanced stages (defined by H&Y stage≥3 and/or LEED>850mg) and 40 healthy controls (HC), represented almost exclusively by cohabitants. Microbiota compositions was studied through 16rRNA amplicon sequencing and classified to taxonomic rank through bioinformatic analysis. A multivariate statistical analysis was performed to identify differential abundant taxa between the three groups (de-novo PD, advanced PD, HC) considering the effect of potential confounding factors, like lifestyle and eating habits.

Results:: The three groups showed differences both in alfa-diversity and in beta-diversity comparisons. We found a progressive reduction in Lachnospiraceae, Bacteroidaceae, Prevotellaceae and Clostridiaceae families moving from HC to de novo PD and finally to advanced PD and a reverse trend in Enterobacteriaceae and Lactobacillaceae families.

Conclusions:: Our study confirms the presence of microbiota alterations from the earliest stages of PD. Furthermore, a greater and more severe alteration in microbiota composition seems to characterize PD advanced stages, highlighting how this non-motor feature progresses with the severity of disease.
WHITE MATTER MICROSTRUCTURAL CHANGES PRECEDING THE DEVELOPMENT OF IMPULSE CONTROL DISORDERS IN PATIENTS WITH PARKINSON’S DISEASE

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Background and Aims:: Impulse control disorders (ICD) can be triggered by dopamine replacement therapies in patients with Parkinson’s Disease (PD). Previous studies have identified several risk factors associated with ICD. In this study we investigated the presence of white matter (WM) microstructural changes at baseline in a cohort of drug-naïve PD patients who successively developed ICD over a 36-month follow-up period (ICD+) compared with patients who did not (ICD-).

Methods:: Baseline 3T MRI images of 48 drug-naive PD patients and 20 matched healthy controls (HCs) were analyzed. The ICD presence and severity at follow-up were assessed by means of the Questionnaire for Impulsive-Compulsive Disorders in Parkinson’s Disease Rating Scale. Diffusion tensor imaging with tract-based spatial statistic analysis was used to evaluate the WM integrity at baseline in 24 ICD+ patients, compared to 24 ICD- and 20 HCs.

Results:: Between-groups analysis revealed a statistically significant increase of radial diffusivity of the main fasciculi of WM in ICD+ compared to ICD- patients. In details, these differences were detectable bilaterally in thalamic radiations, cortico-spinal tracts, inferior longitudinal, superior longitudinal and uncinate fasciculi and in the splenium of corpus callosum.

Conclusions:: We demonstrated, in PD patients who will eventually develop ICD, the presence of WM changes at baseline, in several areas strongly involved in cognitive and behavioural functions, with a central role played in the reward system and motor inhibition. The evidence of early axonal damage may represent a potential biomarker and an additional risk factor for the emergence of ICD in PD patients.
IMPACTS OF CLASSICAL MUSIC AND DANCING ON COGNITIVE FUNCTIONS IN PARKINSON’S DISEASE.

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Background and Aims:: In the modern world, Parkinson's disease is the second most common neurodegenerative disease. And variety of non-pharmacological methods and technologies occupy an important place rehabilitation. To study changes in the cognitive plan among patients with Parkinson's disease after conducting dance classes and listening to classical music based on rehabilitation therapy under the TMA program, evaluate the dynamics of changes in such cognitive functions, memory, speech, attention, etc. according to MMSE and MoCa rating scales

Methods:: Patients were divided into two groups. The first group (n = 27) underwent therapy with rehabilitation therapy with TMA and the control group (n = 26) who received standardized treatment without this program. The lesson was held once a week for 1 hour for 12 weeks at the base of rehabilitation of neurological patients at the TMA clinic. Patients had an early stage of PD without cognitive impairment (Addenbrook score: DG = 92.3 ± 2.7, CG = 90.8 ± 3.9). Both groups took cognitive function tests on the first day of admission, as well as on days 21 and 48.

Results:: Comparison of the results showed that the cognitive functions of patients such as verbal training (= 28%), delay (= 28%), recall delay (= 20%), memory capacity for verbal material (= 12%) improved in relation to the control group. (p <0.05)

Conclusions:: Rehabilitation with the help of dance lessons and classical music have a clear benefit from psychological symptoms, preservation and optimization of cognitive function. Long-term studies are necessary to confirm the persistence of these effects.
COMPARATIVE EVALUATION OF THE EFFECTIVENESS OF GROUP COGNITIVE REHABILITATION AND RELAXATION THERAPY IN PATIENTS WITH PARKINSON’S DISEASE

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Background and Aims:: Compare the effectiveness of group cognitive rehabilitation and relaxation therapy in patients with Parkinson's disease (PD).

Methods:: We examined 20 patients with PD and conducted a prospective, single-blind, randomized clinical trial. Participants passed tests to evaluate cognitive function to assess the presence of mild cognitive impairment or dementia in PD. All patients were divided into two groups by the group of cognitive rehabilitation and relaxation therapy group in random order. CRG participants (n = 12) trained cognitive functions in the perspective of household life. This group focused on strategies for restoring, compensating, and optimizing cognitive brain function. Patients of the second group (n = 8) also performed home training. They underwent music therapy and art therapy. All trainings were 2 times a week for 10 weeks.

Results:: The results showed a significant improvement in CRG demonstrated in verbal learning (by = 28%), retention (by = 28%), delayed recall (by = 20%), memory capacity for verbal material (by=12%). There were significant improvements in the WG that were demonstrated in verbal learning (by = 36%) deferred recall (by = 40%), the amount of memory for verbal material (by = 12%) and the total amount of recall in non-verbal memory (by = 36%).

Conclusions:: Based on the results obtained, it can be concluded that CR does not have a specific effect on short-term memory performance in patients with PD. These requests require further research in the long term because other types of interventions may also be effective in relation to the cognitive functions of patients with PD.
INFLUENCING FACTORS ON COGNITIVE FUNCTION IN PARKINSON'S DISEASE

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Background and Aims:: The cognitive impairment in Parkinson's disease is influenced by many factors, including sleep disturbance. To clarify clinical features of sleep disorders in patients with Parkinson’s disease (PD) and their effect on cognitive function.

Methods:: The study involved 106 patients with PD (55 men and 51 women) mean age 56.04±10.9 years. The control group consisted of 20 patients without Parkinsonism matching by age and sex. The diagnosis of PD was established by criteria A.Hughes. To determine cognitive disorders we used neuropsychological tests.

Results:: 83 patients (78.3%) had sleep disorders. In the structure of sleep disorders: 49 (59.0%) patients had insomnia and 18 (21.6%) patients - parasomnia and 16 (19.4%) - hypersomnia. In a control group, numbers were 4.5 times less. The analysis showed that the structure of sleep disorders correlates with the form of PD. So, insomnia is more rapidly met in akinetic-rigid form (57.5%), whereas hypersomnia is presented in mixed form. Patients with insomnia present 38% of predementia cognitive impairment and 36% of dementia (66.7% of mild degree dementia and 33.3% moderate dementia severity). Whereas, in patients with hypersomnia 35% of predementia cognitive impairment, 60% of dementia (54.6% and 45.4%) were observed. Among patients with permanent drowsiness 32.4% of predementia cognitive impairment and 59.6% of dementia (44.8% and 55.2%) were diagnosed. Dementia (66.7%) was observed more in patients with sudden sleep (42.8% and 57.2%).

Conclusions:: Cognitive impairment in Parkinson's disease does not depend only on the form, stage and duration of the disease, but also depends on sleep disturbance.
CORTICO-SUBCORTICAL FINDINGS IN IDIOPATHIC REM SLEEP BEHAVIOR DISORDER (IRBD) AND PARKINSON'S DISEASE: A VBM STUDY.

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Background and Aims:: Idiopathic rapid eye movement sleep behavior disorder (iRBD) is a parasomnia characterized by the loss of physiological atonia with abnormal behavior during REM sleep. RBD could be the prodromal manifestation of neurodegenerative diseases, such as Parkinson's disease (PD). Neuroimaging studies showed the presence of structural and functional abnormalities involving cortical and subcortical regions in RBD.

Methods:: Patients with iRBD, diagnosed based on thorough clinical interviews and VPSG, were recruited. Patients with PD according to the UK Brain Bank criteria were evaluated with the RBD Single-Question Screen and categorized into PD with RBD (PD-RBD+). A group of healthy controls (HC) were also recruited. Each subject underwent a brain MRI.

Results:: Sixteen patients with iRBD, 13 PD-RBD+, and 30 HC were enrolled. VBM-ANOVA analysis revealed a pattern of grey matter atrophy (GM) from HC to PD-RBD+, involving left middle temporal gyrus. Clusters of GM increase in PD-RBD+ and iRBD were found in bilateral caudate body, midbrain, middle occipital, middle frontal and post central gyri (p<0.05 FWE).

Conclusions:: We found the reduction of GM density in temporal areas with a decreasing pattern of atrophy from PD-RBD+ to HC, and the presence of increased GM volume in basal ganglia structures, together with the involvement of midbrain and cortical structures, with an inverse pattern. According to previous findings showing abnormalities in cortical and subcortical structures involved in REM sleep mechanisms, these data could suggest the presence of a neurobiological link connecting RBD to a-synucleinopathies.
BACKGROUND AND AIMS:: In temperate climates, many factors that may influence function in Parkinson's disease (PD) vary according to season [Ronald B Postuma, 2005]. Goal of our research was the determination of connection between symptoms in patients with Parkinson's disease (PwPD) and seasons.

METHODS:: This study included 204 PwPD, but only 128 got to the end of the research. Some patients left because of severe cognitive impairment, refusals to continue, death. This study was held for 3 years (2018-2020) with patients' examination four times per year: one survey every season. Neurological examination was based on MDS-UPDRS, AIMS, Schedule for the Assessment of Drug-Induced Movement Disorders(SADiMoD), Apathy scale, HADS, Epworth Sleepiness Scale(ESS), SCOPA-AUT, MoCA-test, QUIP-RS, C-SSRS, PDQ-39.

RESULTS:: Increased NMS were observed in off-season: autonomic symptoms($p=0.021$), falls($p=0.026$), hallucinations($p=0.037$), perception problems($p=0.041$), a tendency to sleepiness and fatigue($p=0.031$). One should note there was no change in depression indicators during the seasons to explain these differences. Though some patients indicate that their motor ability is better in summer, no correlation found between MDS-UPDRS subscores and season ($p > 0.05$).

CONCLUSIONS:: Thus NMS in PwPD change throughout the year with symptoms becoming worse in autumn and spring and relieving in summer ($p<0.05$). What concerns motor symptoms they doesn't aggravate in seasons. This should be taken into account when changing treatment regimens and interpreting the clinical trials results. This study should be continued to get more information.
RISK FACTORS FOR FREEZING OF GAIT AND RELATED NON-MOTOR SYMPTOMS IN PARKINSON’S DISEASE

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Background and Aims:: To identify possible risk factors and the anamnestic association of gait freezing (FOG) in patients with Parkinson’s disease (PD).

Methods:: 84 patients with PD were evaluated on the basis of a sample on the following scales: MDS-UPDRS scale, modified Hoehn and Yahr (HY) Stage, MMSE and Clinical Dementia Rating scale. MDS-UPDRS was used to evaluate and determine PIGD, as well as for the Balance-Gait (PIGD minus FOG) score, non-motor symptoms (nM-EDL) and motor complications (MC). To clarify the clinical signs and their relationship with FOG, one-way tests were followed up with subsequent nominal logistic regression (Log Regr).

Results:: 36% of patients had FOG, these cases were associated with stage HY (≥3, p <0.0001), 70% of patients had PIGD. Patients with FOG + more often had MC and a higher equivalent dose of levodopa (LED) (p <0.0001) compared with PIGD / FOG patients, PIGD / FOG + patients had a longer duration of PD duration during the disease, a higher score of Bal-Gait, a higher indicator of LED, a higher frequency of psychosis, they are more likely to have dyskinesia, a higher rate of impact on motor vibrations and a general deviation from the norm and problems with urination, while differences in cognitive status were not significant.

Conclusions:: It can be said that for in PD the obvious factors for the development of FOG are PIGD, MC / LED and Cog impairment. Their nature may be additive in its effect. Patients with FOG more pronounced motor dysfunctions, in particular Balance-Gait disorder are more characteristic.
COULD THE ANESTHETIST IMPROVE THE MOVEMENT DISORDERS SPECIALIST JOB?

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Background and Aims:: Deep brain stimulation (DBS) is a neurosurgical procedure consisting in implant of electrodes in specific brain areas to improve clinical outcome of some neurodegenerative disorders i.e. Parkinson disease (PD). No clear data are available about what is the best anesthetic protocol in those patients. This study aims at demonstrating the impact of the anesthetic protocol choice on outcomes of DBS in patients affected by PD.

Methods:: We performed a prospective analysis on patients affected by PD who underwent DBS between March 2013 and October 2015. They were divided in two groups on the bases of the anesthetic protocol used during the procedure: group A for Propofol-Dexmedetomidine and group B for Propofol-Ramifentanil. We analyzed a series of factors such as vital signs during surgery, surgical time, micro-recording data, surgical complications, UPDRS III before and at the end of the procedure, days of Hospital discharge, and the delta levodopa equivalent daily doses.

Results:: We included 19 patients, with a mean age of 57 ± 5 years; 10 of them were included in Group A. We found that in group A the days of Hospital discharge (p-value 0.0355) were significantly less, as well as the surgical time (p-value 0.0300) compared to those found in the Group B.

Conclusions:: The study shows that patients undergone Propofol-Dexmedetomidine protocol had lower surgical time and less days of hospitalization, and that means a more rapid recovery from surgery compared with patients undergone Propofol-Ramifentanil protocol.
TECHNOLOGY USE IN PARKINSON'S DISEASE AND PARKINSONISM: A MULTICENTER SURVEY IN REAL-LIFE HEALTHY EAST LOMBARDY PARKINSON (HELP-)NETWORK

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Background and Aims:: Background: technology use is increasing in the ageing population but no large studies evaluated the access to internet and digital technology in parkinsonian patients. Objective: to evaluate the real-life use of internet and technological devices in parkinsonian patients

Methods:: a real-life survey in a network of movement disorder outpatient clinics in Lombardy Region, Italy was conducted. Consecutive Parkinson’s disease (PD) or atypical parkinsonism patients were asked to complete a standardized questionnaire evaluating the use of technology, internet and devices; the severity of the disease and milestones of disability were evaluated in the cohort.

Results:: Four hundred-fifty-four patients in 11 centres were included (mean age 70.5 + 9.7 years, mean dis duration 7.1 + 5.2 years), namely 411 PD (16.3% with dementia and 44% with motor fluctuations) and 43 atypical parkinsonism. 43% PD and 23.7% of atypical parkinsonism had access to email with a mean use of 6.4 hours per week. 75% of patients had smartphone 12% tablet and 14% computer with no difference between patients with and without motor fluctuations. OFF-line patients were older and exhibited worse motor and non-motor symptoms compared to patients with internet access.

Conclusions:: the survey highlighted an heterogeneous use of digital technology and internet in the population. The wide global internet access, prominent via smartphone highlight its potential for monitoring symptoms in clinical routine or in clinical trials. OFF-line patients have an increased risk of disability thus requiring specific interventions from clinicians and health care systems.
Background and Aims:: Especially in recent years, there has been increased interest in the clinical use of brain markers such as S100B proteins. To study the activity of the protein S100B in the blood serum of patients with striatal hyperkinesis (SH), depending on the duration of disease.

Methods:: The material of this study was 42 patients receiving inpatient and outpatient treatment in the 1-Republican Clinical Hospital Ministry of Health of the Republic of Uzbekistan. Patients ranged in age from 36 to 66 years (mean age 52.4±7.6 years). Duration of the disease is 1 to 8 years.

Results:: The study on the content of S100B serum of patients with secondary SH level was increased, while in the basic group was 116.2±5.8 ng/l and the control group, 72.6±2.6 ng/l (p<0.05). We conditionally allocated patients into 3 groups depending on the duration of the disease: one group of patients, the duration ranged from 6 months to 1 year, 2 patients from group 1 to 3 years and 3-band more than 3 years. These results show that the level S100B serum depends on the duration of the disease, whereas the duration of more than 3, the level of the protein was observed at a higher level than the duration of 6 months to 1 year, 112.4±5.6-153.7±6.8-178.7±6.5 ng/l, respectively. In primary striatal hyperkinesis, the protein S100B level was closer to the control group, 86.5±1.1 ng/l

Conclusions:: Serum S100B activity in patients with secondary hyperkinesis indicates the influence of serum factors that are already in the early stages.
CANNABINOIDS’ NEUROPROTECTIVE EFFECT AS AN ALTERNATIVE TREATMENT FOR PARKINSON’S DISEASE: A SYSTEMATIC REVIEW

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Background and Aims:: Parkinson's disease (PD) is a neurodegenerative disease caused by the deterioration of substantia nigra pars compacta’s dopaminergic pathways, resulting in a decrease in stimulation of the motor cortex and symptoms linked to the reduction of automatic movements. It is known that several substances have protective effects against PD, among them cannabinoids (CB), obtained from Cannabis sativa, with emphasis on Cannabidiol (CBD) and Δ⁹-tetrahydrocanbinol (Δ⁹-THC). The aim of this study was to assess previous data describing the protective role of cannabinoids in PD and their mechanisms of action, focused on improving symptoms and quality of life of individuals with the disease.

Methods:: Searches in PubMed and PMC were performed and articles published within the last 5 years that described protective effects of cannabinoids in individuals with PD, addressing their mechanism of action, were included.

Results:: Until now, 179 articles that establish a link between cannabinoids and PD were found. Their initial analysis revealed significant neuroprotective effect, but the mechanisms of action of CB in the central nervous system, which contribute to the regression of PD, still vary and there is no consensus on which theory is the most acceptable.

Conclusions:: The literature that reports the effects of PD cannabinoids is not conclusive, but studies show that there is a connection between the activation of cannabinoid pathways, Parkinson's disease and BDNF production that can be explored to obtain favorable clinical outcomes. Future studies are necessary to determine which of these substances’ mechanism of action actually guarantees their protective effect against neurodegeneration.
HYPOGLYCEMIC ENCEPHALOPATHY MANIFESTING WITH HEMIBALLISMUS AND CONTRALATERAL CORTICAL FRONTO-PARIETAL LESIONS

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Background and Aims: Severe hypoglycemia is associated with a broad range of neurological deficits and alterations on cerebral magnetic resonance imaging (MRI). Typically, hypoglycemic encephalopathy causes symmetrical lesions to the cerebral cortex, with temporal lobes and basal ganglia appearing most susceptible. Cortical involvement usually correlates with a poor functional outcome.

Methods: A 71-year-old man was admitted to hospital for acute hypoglycemic coma in poorly controlled type 2 diabetes mellitus. He promptly regained consciousness after intravenous glucose administration but during hospitalization he developed prominent intermittent ballistic movements of his right limbs intermixed with rare distal choreic movements. The involuntary movements did not respond to anticonvulsants and subsided within 12 days since admission in parallel with the improvement of glycemic control. Four months later, his neurological examination was normal.

Results: At hospital admission, CT brain scan was normal. Serial EEGs registered during the atypical movements failed to note any epileptic activity. Brain MRI showed left fronto-parietal cortical-subcortical T2-hyperintense lesions, with cingulate gyrus involved. DWI and T2-FLAIR sequences were hyperintense, ADC was reduced. Follow-up MRI imaging showed progressive regression of the abnormalities. After 80 days, cerebral MRI was normal.
Conclusions: This is the first report of cingulate gyrus damage in hypoglycemic encephalopathy. Unilateral cortical involvement could be explained by a generalized asymmetry of the cerebral vascularization. This is also the first evidence of pure cortical dysfunction in hypoglycemia-induced hemiballismus. This case also suggests that certain patients with cortical involvement in hypoglycemic encephalopathy may present a good clinical outcome, likely, if normal glycemic levels are promptly restored.
Background and Aims:: Markers for early detection of striatal hyperkinesis (SH) has not yet been fully explored not only in Uzbekistan, but in others the efforts of the world.

To study the basic clinical and non-clinical factors affecting the quality of life of patients with SH.

Methods:: The study involved 62 patients with SH (32 men and 30 women) and the control group consisted of 20 patients without SH. All patients underwent clinical neurological examination, including a detailed assessment of movement disorders. To evaluate the quality of life was used the EuroQoL-5D.

Results:: Compared with patients with SH motor and non-motor disorders significantly affect quality of life. It was found that 35 patients (56,4%) with SH have addressed to the doctor after 4-6 years from the onset of the disease, 19,3% (12) patients with SH were not even examined by specialized doctors, 24.3% (15) patients with SH had never applied to see a doctor. Among patients with SH who did not go to the doctor motor changes occurred in 92.3% of cases, pain/discomfort 85.1%, and anxiety/depression in 87.7% of cases, these rates among patients go the doctors amounted to 84.3 %, 78.4% and 76.2% respectively, and have created some problems (p<0,05). One of the factors affecting the quality of life is the late diagnosis of undifferentiated and SH.

Conclusions:: The deterioration of the quality of life of patients with SH depends on clinical factors in the form of motor and non-motor disorders, late treatment of patients to the doctor, undifferentiated and late diagnosis, untimely differential treatment.
**Background and Aims::** One of the most common circadian rhythm disorders in Parkinson's disease is a sleep cycle disorder.

**Methods::** A special questionnaire was developed to assess sleep disorders in Parkinson's disease (PD) and Vascular parkinsonism (VP). The study included 47 patients with PD and 40 patients with VP. Patients were divided into two groups and one group was recommended only basic treatment, while the second group was recommended 3mg of melatonin 40 minutes before bedtime. Patients' results were analyzed using scale of assessment of sleep disorders in modified PD and MMSE scale during four-week period.

**Results::** Prior to treatment, insomnia was observed in both groups, in the PD and VP patient groups. The addition of melatonin therapy to the main treatment provided significant efficacy, with an efficacy of 16% observed in the first week and was almost 10%, whereas in the second week it was higher efficacy of 26%, and in week 4 there was an increase in efficacy to 39%. Among VP patients melatonin therapy showed high efficacy in monitoring, with an efficacy of 10% after the first week of treatment, 19% after the second week, 32% after the third week, and 45% after the fourth week. Before treatment MMSE score was 21.3 ± 3.2 for PD patients and 24.3 ± 3.2 for PD patients receiving basic treatment, and 26.4 ± 2.1 for patients receiving basic treatment + melatonin therapy. And patients with VP the mean MMSE score before treatment was 20.4 ± 4.4, and 23.1 ± 3.2 in patients receiving basic treatment, patients receiving basic treatment + melatonin therapy had a mean MMSE score of 27.4 ± 2.1.

**Conclusions::** The results show that adding melatonin therapy to basic treatment for circadian rhythm disorder in PD and VP improves treatment efficacy and prevents deepening of cognitive impairment.
FROIN SYNDROME- A RARE MIMIC OF SPINOCEREBELLAR ATAXIA

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Background and Aims:: Spinocerebellar ataxias are degenerative heritable disorders affecting cerebellum accompanied by changes in brainstem and other parts of central nervous system. This case highlights the same and emphasizes on the importance of recognizing clinical and radiological clues for identification of secondary causes of cerebellar degeneration for timely intervention and management of patient.

Methods:: We present a 52-year-old female with 10-year history of progressive frontal predominant behaviour disturbances in form of apathy and impaired judgement accompanied with progressive pan cerebellar involvement and spastic quadriparesis with urinary incontinence. Her MRI brain showed diffuse cortical and cerebellar atrophy with communicating hydrocephalus with irregular wavy borders of dilated sylvian fissure and low signal with blooming seen along cortical and cerebellar sulci. Further CSF showed xanthochromia with raised csf protein. Provisional diagnosis of spinal cord tumour with secondary superficial hemosiderosis was kept and MRI spine was done which showed T2 heterogenous hyperintense lesion in spinal cord opposite lumbar (L1-L2) vertebrae which was removed.

Results:: The spinal cord lesion removed was diagnosed as Grade 1 myxopapillary ependymoma on histopathology with secondary froin syndrome and superficial hemosideros. On followup, patient's behaviour changes and spasticity has improved though her cerebellar signs persist.

Conclusions:: It is important to always have high degreee of suspicion for treatable causes of chronic progressive cerebellar dysfunction especially when accompanied by other signs of neuraxis involvement and subtle imaging findings.
SACCADIC BRADYKINESIA IN PARKINSON’S DISEASE: PRELIMINARY OBSERVATIONS

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Background and Aims:: Bradykinesia and hypokinesia of limb movements are features of Parkinson’s Disease (PD), exacerbated when patients perform self-guided, repetitive limb movements— the so-called ‘sequence effect’. In the oculomotor system, both hypometria and slowing of voluntary saccades have been described in PD (1) but never as a change over time, which is the defining feature of this phenomenon.

Methods:: We examined six mildly- or moderately-impaired PD patients (Unified Parkinson’s Disease Rating Scale: UPDRS motor part, 11±2.8 points; duration of illness, 2.2±0.4 years) aged 69±5 yrs (one female) and seven age-matched healthy control individuals (five female, 56±7 years). Voluntary and reflexive horizontal saccadic eye movements were recorded with infrared binocular videonystagmography (VNG) sampled at 250Hz.

Results:: Voluntary horizontal saccades without visual targets led to a progressive decrease in PD saccadic amplitude over time (hypometria). Additionally, PD saccadic velocity progressively reduced over time, even when accounting for smaller saccadic amplitudes main sequence effect. Group (PD vs. Controls) and time (first six vs. final six saccades) interacted for both amplitude and velocity (F(1,11)>6.1; p<0.0031), with a decrease over time in PD (p≤0.001) but not controls (p>0.110). PD saccadic velocity in the final six saccades was lower than normative amplitude-matched velocities (p=0.039) whereas no difference was present in the first six saccades (p=0.547).

Conclusions:: Saccadic bradykinesia was apparent in all consecutive patients, but absent in age-matched controls. “Saccadic bradykinesia” may be a useful and early clinical sign of PD and future studies should confirm these findings and assess its specificity as a clinical biomarker of disease progression.
ASPECTS OF THE VEGETATIVE DISORDERS OCCURRENCE IN THE PARKINSON'S DISEASE AND VASCULAR PARKINSONISM

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Background and Aims:: Vegetative disorders are among the most common and diagnostically significant disorders in Parkinson’s disease(PD) and Vascular Parkinsonism(VP) after motor disorders.

Methods:: A clinical neurological examination was carried out in 47patient with PD and 40with VP who hospitalized in the Department of Neurology of the TMA. A special survey was carried out, the results of the survey were analyzed.

Results:: According to the results of the survey, the incidence of general hyperhidrosis was predominant in the group of PD patients and consisted 74.4%. In the group of VP patients total hyperhidrosis was observed in 7.5%, constipation was observed in 64% patients with PD, in VP patients this figure was observed in VP patients this figure was 10%, similarly, salivation was high in PD patients, in 46.8% of cases, in VP it was observed in 3 patients, ie in 7.5% of cases, and orthostatic hypotension was observed in high indicators in the group of VP patients. It has been suggested that the observation of idiopathic orthostatic hypotension in the VP group with a high frequency is related to the changes observed in the blood vessels. Similarly, angiotrophalic changes were observed in 42% of patients in the VP group and in 7% of patients in the PD.

Conclusions:: Although Peripheral Vegetative Deficiency Syndrome occurs in both diseases, it manifests in two forms of the disease in terms of origin and appearance. These changes are important in the diagnosis of the disease.
ASPECTS OF METABOLIC DISORDERS IN PARKINSON'S DISEASE, VASCULAR PARKINSONISM AND CHRONIC CEREBRAL ISCHEMIA

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Background and Aims:: Although the origin of Parkinson’s disease is not the result of a metabolic disorder, metabolic acceleration plays an important role in the development of this disease and the development of motor symptoms. To identify and analyze the features of metabolic disorders in Parkinson's disease, vascular parkinsonism and chronic cerebral ischemia

Methods:: Anthropometric analysis and bioimpedensitometry were performed in 47 patients with Parkinson's disease (PD), 40 with Vascular parkinsonism (VP) and 30 with Cerebral chronic ischemia (CCI) to found metabolic disorders in PD, VP, CCI.

Results:: It found that, in the group of patients with PD, in 32% BMI was <18.5 below, and in 53% of patients BMI was between 18.5 and 24.9, and in 15% of patients BMI was above 25. In 15% of patients with VP, the BMI was less than <18.5, in 30%, the BMI was in the range of 18.5–24.9, and in 65%, the BMI was higher than 25. In the group of patients with PD, in 31% of patients muscle mass was 46.1 ± 1.76, in 50% of patients muscle mass was 48.1 ± 1.40 and in 19% of patients 64,664.6 ± 1.8. In 18% of patients with VP, muscle mass was 54.0 ± 1.02, in 61% of patients muscle mass was 51.1 ± 1.39, and in 21% of patients, muscle mass was 49.9 ± 1.36. In the CCI group of patients muscle mass averaged 47.0 ± 1.02.

Conclusions:: The results obtained show that a decrease in muscle mass in Parkinson's disease is less common than in vascular parkinsonism and chronic cerebral ischemia.
Background and Aims:: Essential Tremor is one of the common causes of tremor affecting elderly worldwide. It is believed to be genetically inherited. Many cases seem to be familial. About half of the cases are due to a genetic mutation and the pattern of inheritance is most consistent with autosomal dominant transmission. Objective: to study the demographics of patients with ET in a tertiary hospital in Penang, Malaysia whether there are any sporadic cases, or solely genetically linked and mainly affect elderly.

Methods:: This is a retrospective analysis of patients with ET from 1988 -2020.

Results:: A total of 159 patients were identified as having essential tremor. There were 43% (n=68 ) males and 57% (n=91 )females. The racial distribution was Malay 20%, Chinese 64% and Indian 15%. The age of patients ranged from (19 - 89) years with a majority (55.9%, n=89) within the age group of > 61 years. 77.35% of the cohort had tremors on their right hand, while 46 patient had titubation. Among the 159 patients, 11.32% (n = 18), not received any treatment, 53 patients are taking propanolol only, 10 patients received primidone monotherapy, 0 patients received 2 drugs (propanolol and primidone). 3 patients has PD superimposed with ET Total 9 patients on clonazepam but 6 patients on Clonazepam as mono therapy while 3 patients on proponolol and clonazepam.

Conclusions:: Our study found that ET is significantly higher among Chinese race with female predominance. A combination of treatment with beta blockers or Phenobarbitals (Primidone) have led to improvement in symptoms.
CSF LEVEL OF ANTI-AGING PROTEIN A-KLOTHO IS INVERSELY ASSOCIATED WITH A-SYNUCLEIN IN PARKINSON’S DISEASE PATIENTS

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Background and Aims:: α-Klotho (KL) is an “anti-aging” protein involved in several age-related and neurodegenerative disorders. However, its role in Parkinson’s disease (PD), especially in vivo, is still poorly explored.

Methods:: We assessed the level of KL, α-synuclein and other neurodegenerative biomarkers, amyloid-β42 and amyloid-β40 (Aβ42 and Aβ40), total tau and phospho-tau181, in cerebrospinal fluid (CSF) of 36 PD patients and 9 control subjects, affected by other neurological diseases.

Results:: CSF KL was increased in PD compared to controls (689±193 pg/ml vs 527±225; p<0.05), independently from age and sex; as expected, CSF α-synuclein was decreased in PD patients compared to controls (PD 943±184 pg/ml; control 1186±249; p<0.005). Levels of Aβ42, Aβ40, total tau and phospho-tau181 were similar in both groups. We found that CSF KL levels and α-syn were inversely associated, suggesting a greater KL expression in those patients with more severe brain synucleinopathy, measured by the reduction of CSF α-synuclein. No correlations between KL and other biomarkers or clinical parameters were found.

Conclusions:: In PD, KL level is increased and may have a neuroprotective role to counteract accumulating synucleinopathy.
ROLE OF OLFACTORY AND GUSTATORY DISFUNCTIONS IN THE REGULATION OF BODY WEIGHT IN PATIENTS WITH PARKINSON’S DISEASE

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Background and Aims:: Parkinson’s disease (PD) is a neurodegenerative disorder characterized by motor symptoms bradykinesia, rigidity, tremor and postural instability. However, PD is usually associated with non-motor symptoms (NMS) that include olfactory and gustatory dysfunctions, neuropsychiatric symptoms such as apathy, anxiety and cognitive impairment, sleep problems, and autonomic dysregulation. Few data are available regarding the contribution of NMSs and motor symptoms on body weight change in PD patients. The aim of this study was to assess the effect of olfactory and gustatory dysfunction, apathy, fatigue and motor symptoms on weight regulation in PD patients.

Methods:: We analyzed 112 participants, 63 PD patients (mean age ± SD, 69.2 ±10.1), and 49 controls (mean age ± SD, 68 ± 9.6). For each participant we collected age, weight, height, olfactory and gustatory function, cognitive performance, apathy and fatigue.

Results:: Our data showed that 61.9% (n = 39) of PD patients had hyposmia, while 38.1% (n = 24) had anosmia. In PD patients, we observed a significant effect of Unified Parkinson’s Disease Rating Scale (UPDRS), apathy, odor threshold, sweet perception and fatigue on body weight regulation. Instead, there was no significant effect for levodopa equivalent daily dosage (LEDD).

Conclusions:: Our results suggest that in PD non-motor symptoms such as olfactory, gustatory, deficits and mood disorders may influence body weight. This study may provide better knowledge in PD patients on the mechanism underlying food intake and weight regulation.
EFFECT OF VITAMIN B12, FOLATE, AND ENTACAPONE ON HOMOCYSTEINE LEVELS IN LEVODOPA-TREATED PARKINSON’S DISEASE PATIENTS: A RANDOMIZED CONTROLLED STUDY

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**Background and Aims:** Previous studies have suggested a significant increase in plasma homocysteine (Hcy) levels in levodopa-treated Parkinson's disease (PD) patients, and vitamin B12 and folate supplementation may decrease Hcy levels. However, the effects of catechol-O-methyltransferase inhibitors on levodopa-induced increase in Hcy levels were conflicting. The aim of this study was to evaluate whether Hcy levels are increased in levodopa-treated PD patients and to evaluate the effects of vitamin B12 and folate or entacapone on Hcy levels in levodopa-treated PD patients.

**Methods:** We analyzed and compared plasma Hcy levels in 20 levodopa-naïve PD patients and 42 levodopa-treated PD patients, followed by randomized assignment of 42 levodopa-treated patients to treatment groups with either vitamin B12 and folate, entacapone, or no medication.

**Results:** Plasma Hcy levels in levodopa-treated PD patients were higher than those in the control group, but the difference was not statistical significant (15.25 ± 6.70 and 13.13 ± 4.68, P = 0.216). Patients treated with vitamin B12 and folate had a significant decrease in plasma Hcy levels (P < 0.001). In the entacapone group, Hcy levels were mildly decreased, but the change did not reach statistical significance.

**Conclusions:** Levodopa-treated PD patients had higher plasma Hcy than levodopa-naïve PD patients. Unlike entacapone, combination supplementation with vitamin B12 and folate was associated with significantly decreased plasma Hcy. We suggest that plasma Hcy levels should be monitored during levodopa treatment, and supplementation with inexpensive vitamin B12 and folate is beneficial for levodopa-treated patients.
ASYMMETRY IN SACCADIC EYE VELOCITY AND LATENCY MAY DISTINGUISH CORTICOBASAL DEGENERATION FROM OTHER ATYPICAL PARKINSONISMS

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Background and Aims:: Corticobasal degeneration (CBD) is a neurodegenerative condition exhibiting a notable overlap in clinical and pathological characteristics with other atypical parkinsonisms. Several eye movement abnormalities have been described in patients with CBD; however, oculomotor signs are variable and often resemble those of other parkinsonian disorders. This study aimed to define the distinguishing patterns of eye motility dysfunctions in CBD patients compared to other atypical parkinsonisms.

Methods:: This study screened patients having diagnosis of atypical parkinsonisms including CBD, according to the diagnostic criteria. All patients underwent a complete neuroophthalmological examination and the video-oculography (Eyelink®1000 Plus), consisting of three eye motility tasks in order to evaluate fixation, smooth pursuit and saccades.

Results:: A total of 11 patients with CBD (4 males [36.4%], age 67.3±7.2 years) and 33 parkinsonian syndromes, including 23 (69.7%) progressive supranuclear palsy (PSP) and 10 (30.3%) multiple system atrophy (MSA), were enrolled. The inter-eye differences (ID) for saccadic velocity and latency were higher in CBD patients compared to PSP and MSA (91.1±63.1 versus 17.1±23.5 and versus 8.4±9.0, p<0.001; 65.9±64.1 versus 16.3±21.6 and versus 18.4±24.6, p<0.001, respectively). Receiver-operating characteristics (ROC) analysis showed that an ID for velocities measurement >20°/s distinguishes CBD from other parkinsonisms with a sensitivity of 90.9% and a specificity of 90.6%, and the area under the ROC curve was calculated as 0.98 (95% CI 0.95-0.99, P < 0.001).

Conclusions:: CBD exhibit distinct oculomotor features. The asymmetrical involvement of saccadic abnormalities may help to distinguish CBD from PSP and MSA.
Changes in Personality Associated with Deep Brain Stimulation in Parkinson Disease

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Background and Aims: Subthalamic deep brain stimulation (STN-DBS) is an effective treatment option in Parkinson's disease (PD), producing robust motor improvements in the motor symptoms and allowing the reduction of antiparkinsonian drugs dosage. There is, however, increasing evidence that STN-DBS may be associated with a higher incidence of adverse changes in behavior when compared to other stimulation sites (1). To date, no study has investigated the effect of the amount of total electrical energy delivered (TEED) on behavioral adverse changes. To characterize this issue, we assessed personality traits correlated with TEED in twenty PD patients before and 12 months after the start of neurostimulation.

Methods: 20 PD patients (12 women, mean [±SD] age 57.6±7.6 years) with advanced L-dopa responsive PD were included in this study. We tested psychological issues before and 12 months after bilateral DBS-STN. To assess personality we used MMPI-2 according to CAPSIT-PD procedure (2).

Results: After 12 months, patients showed a significant increase only in MMPI-2 subscale D for depression (preDBS mean: 55.43, SD:8.95; 12 Months mean:61.73, SD:10.15; p=0.0053, r=-0.41, Wilcoxon signed-rank test). All the other subscales did not differ before and after 12 months DBS. We found a correlation between the changes in MMPI-2 subscale D after 12 months and TEED on the right hemisphere (Spearman's rho=-0.68, p=0.007).

CLINICAL FEATURES OF PRIMARY PARKINSONISM TAKING INTO ACCOUNT THE RESULTS OF MOLECULAR-GENETIC DIAGNOSTICS

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Background and Aims:: INTRODUCTION. Parkinson's disease (PD) is a progressive neurodegenerative disease, which is based on a decrease in the number of dopaminergic neurons in the substantia nigra. Genetic defects of the PARK2 gene are responsible for the development of 50% of cases of autosomal recessive juvenile parkinsonism (JP) and 10-20% of PD with early onset. The gene LRRK2 is the second most important gene, mutations in which cause the development of autosomal dominant and sporadic forms of PD. PURPOSE OF THE STUDY. Study of clinical features taking into account the results of molecular genetic diagnostics of patients with primary parkinsonism (PP).

Methods:: METHODS. Family history data, neurological status, results of molecular genetic diagnostics were examined - PCR, sequencing, denaturing high performance liquid chromatography, restriction analysis.

Results:: RESULTS. The group of patients with PP consisted of 62 people: 60 with PD (of which 35 PD with early onset before the age of 45 years) and 2 patients with JP. The prevalence of women among all patients was revealed; their ratio with men was 1.1: 1. The age of the examined persons was from 27 to 77 (52.1 to 19.3); the age of onset of the disease was from 19 to 72 years (44.9 11.2). In the group of PD patients with early onset: age from 27 to 74 (47.29.5), age of onset of the disease from 22 to 45 years (37.3 to 7.1).

Conclusions:: The group of patients with PP consisted of 62 people: 60 with PD and 2 patients with JP
QUALITY OF LIFE OF PATIENTS WITH PARKINSON'S DISEASE AND THEIR CAREGIVERS DURING THE COVID-19 PANDEMIC

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Background and Aims:: The coronavirus disease 2019 (COVID-19) pandemic has negatively affected the mental health of the general population. The determinants of quality of life (QOL) in Parkinson’s disease (PD) patients and their caregivers during the COVID-19 pandemic were assessed.

Methods:: We performed a single center, cross-sectional study including 100 patients with PD and their caregivers/spouses. The Hospital Anxiety and Depression Scale was used to assess anxiety and depression. To assess health-related QOL, the physical component summary (PCS) and mental component summary (MCS) scores of the short form (SF)-8 were used.

Results:: Regarding health-related QOL, physical function, role physical, general health, vitality and the PCS score were significantly worse in PD patients than in caregivers. Worsening of PD-related symptoms, increased stress, and decreased physical activity were observed in 29.0%, 37.0% and 44.0% of PD patients, respectively. Sixteen patients (16.0%) experienced problems accessing the hospital, but none reported medication shortages. Approximately half of the participants had strong concerns about COVID-19. In PD patients, increased gait disturbance and rigidity, disease severity, smoking, the levodopa equivalent dose and decreased body weight predicted a worse PCS score, while anxiety, depression, female sex, stress and long disease duration predicted a worse MCS score. In caregivers, age and smoking contributed to a worse PCS score, while depression, stress and worsening patient mood contributed to a worse MCS score.

Conclusions:: We showed the negative impacts of the COVID-19 pandemic on health-related QOL and its determinants in PD patients and their caregivers.
AFFECTIVE DISORDERS AND QUALITY OF LIFE IN PATIENTS WITH CERVICAL DYSTONIA REGULARLY TREATED WITH BOTULINUM TOXIN

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Background and Aims:: Cervical dystonia (CD) is the most common type of dystonia. Anxiety and depression affects up to 70% of patients with CD and markedly reduce health-related quality of life. The most effective method of treatment of CD is local injections of botulinum toxin. Reduction of motor symptoms should improve not only motor symptoms, but also decrease the severity of depression, anxiety and increase quality of life. Aim: To evaluate quality of life, anxiety and depression in patients with CD regularly treated with botulinum toxin.

Methods:: 10 patients (6 females and 4 males) with mean age 41,4±5,1 years were assessed. The severity of CD was assessed using Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS), quality of life - by SF-36, affective disorders – by Beck depression inventory and Silberger anxiety inventory. Second assessment was performed in 2-4 years after regular treatment with botulinum toxin.

Results:: Severity of CD (TWSTRS) decreased from 39,0±8,0 to 29,9±6,5 (p<0,05). Physical component of SF-36 decreased from 41,1±7,5 to 34,9±10,7 (p<0,05)

Conclusions:: Regular treatment of CD with botulinum toxin improved physical component of the quality of life, which corresponds to the improvement of the overall severity of CD. However, no changes in the severity of the affective disorders were noticed, moreover mental health component of SF-36 worsened in the half of the patients. Psychological changes seem to play an important role in the health-related quality of life in patients with CD. They do not respond to the treatment of motor symptoms of CD and probably have more complex etiology than physical presentation.
A PILOT RANDOMIZED TRIAL OF MOBILE-HEALTH DELIVERED REHABILITATION FOR PARKINSONS DISEASE IN GHANA

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Background and Aims:: In addition to dopaminergic drug therapy, rehabilitation is key component of holistic Parkinsons disease (PD) management strategy. Rehabilitation however is severely constrained in sub-Saharan Africa (SSA) due to access barriers. We sought to assess the comparative efficacy of a domiciliary mobile health telerehabilitation intervention vs in-person rehabilitation among patients with PD in Ghana.

Methods:: A pilot randomized clinical trial was conducted at the Neurology clinic at the Komfo Anokye Teaching Hospital in Kumasi, Ghana. Eligible participants were PD patients with Hoehn and Yahr stage 1-3. Participants were randomized to either the telerehab intervention administered daily for 5 days a week for 3 months using the 9zest App on a Smartphone vs usual care i.e. in-person rehabilitation as determined by physician/physiotherapist. Primary outcomes were change Unified Parkinsons Disease Rating Score (UPDRS) II-III and PDQ-39 Summary index at month 3.

Results:: 26 participants were allocated to the intervention vs 30 to usual care with median ages of 60 years vs 64 years respectively, p=0.03. At month 3, the mean change in UPDRS II-III scores was -1.76 ± 7.37 on the intervention vs -0.83 ± 5.43, p=0.59 while PDQ-39 summary index was 13.1% ± 10.0 on the intervention vs 19.9% ± 12.7 in the usual care, p=0.03. Participants on the telerehab arm reported good to excellent satisfaction with the intervention.

Conclusions:: We demonstrate feasibility and comparable preliminary efficacy of telerehabilitation for PD in a resource-limited setting. Wider scale testing of this promising intervention across low-and-middle income countries is warranted.
INCOMPLIANCE IN LONG-TERM TREATED PATIENTS WITH NEUROLOGICAL WILSON’S DISEASE

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Background and Aims:: This study aimed to analyze the compliance in long-term treated patients with neurological Wilson’s disease (WD).

Methods:: Retrospective chart analysis of 112 patients with diagnosed WD who were seen in the outpatient department of the university hospital in Düsseldorf (Germany) on a regular basis over the last 35 years. Clinical neurological scores and repeated laboratory testings were analyzed.

Results:: Duration of follow-up ranged from 1 to 35 years. During the first two years after diagnosis patients were seen between 1 to 4 times per year in the out-patient department. Thereafter frequency of contact declined to 1/year during the next 5 years and to 1/2years during the next 5 years. The severity of neurological symptoms rapidly improved during the first three years and then remained stable. In parallel, excellent liver recovery was observed. Most patients were continuously compliant in adhering to the visit schedule and treatment regimen. However, about 25% of the patients presented with considerable variability of laboratory findings, indicating reduced compliance. The presence of psychiatric symptoms appeared to be a risk factor for incompliance. One patient died after he had stopped medication for one year.

Conclusions:: After rapid initial improvement of neurological symptoms the long-term outcome is stable, but careful monitoring of therapy is recommended because of possible incompliance, especially in patients with psychiatric symptoms.
A (VERY) EARLY ONSET PARKINSONISM

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Background and Aims:: A 51 years-old woman was admitted to our Neurology department, because of poor control of her Parkinson’s disease’s (PD) symptoms. Her history started when she was 11 years old, with an abrupt onset of gait disturbances and a dystonic posture in the left lower limb. She then progressively developed bilateral arm tremor and axial rigidity. She was diagnosed with PD at the age of 24, and then started dopaminergic medication, still ongoing. Her personal history revealed a 30 years old-psychiatric disorder treated with neuroleptics. Her father presented cognitive impairment.

Methods:: At our clinical examination, she was presenting with unpredictable motor and non-motor levodopa-induced fluctuations, namely dystonic postures during the OFF-state and lower limbs dyskinesia during the ON-state. The presence of a fixed dystonic posture of left lower limb and facial-facial-finger myoclonus were also detected. We performed a brain MRI, showing diffuse cerebral atrophy, and an extensive neuropsychological evaluation showing multiple cognitive deficit (MMSE 21.31).

Results:: Given the early symptoms onset, the presence of motor and non-motor features and the family history, we performed a next generation sequencing genetic testing, which revealed a double heterozygosis within the ATP13A2 gene (PARK9). These mutations have not been described yet and are potentially diagnostic for a Kufor-Rakeb syndrome (KRS).

Conclusions:: This case highlights the importance of considering genetic testing in the presence of family history for neurological disorders as well as early onset and occurrence of both motor and behavioral disturbances. The presence of facial-facial-finger myoclonus is a clue clinical sign suggesting the diagnosis of KRS.
APPLICATION OF TEMPORHYTHMIC CORRECTION NEUROREHABILITATION EXERCISE COMPLEX IN PARKINSON'S DISEASE

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Background and Aims: Temporhythmic correction (TRC) is a new complex of neurorehabilitation exercises used in Parkinson’s disease. In this method, exercises that develop fine motor skills are performed with music.

Methods: The effectiveness of TRC was evaluated in the Department of Neurology of the Clinic of the Tashkent Medical Academy in patients with a diagnosis of Parkinson's disease. Patients were divided into 2 groups: the first group received only basic treatment, the second group received basic treatment + TRC. In patients, TRC was performed for ten days. Step length was measured before and after treatment. A special survey was conducted to assess the level of quality of life.

Results: The mean step length was 57.3 before treatment in the first group and 61.2 after treatment. In the second group, it was 56.3 before treatment and an average of 70.4 after treatment. According to the survey, 67% of patients after TRC had a decrease in tremor frequency, 72% had a decrease in rigidity, 69% had improved sleep quality, 58% had improved self-care, and Decreased difficulty in stepping was observed in 56% of patients. 53% of patients felt that no mood disorders were observed after TRC. Muscle tone normalized after TRC in 32% of patients.

Conclusions: TRC is effective in all types of Parkinson's disease, improves quality of life in patients, increases the effectiveness of drug treatment. TRC effectively treats gait and movement disorders in patients, and improves sleep quality.
BOTULINUM TOXIN A AND CERVICAL DYSTONIA: A LONG-TERM MONOCENTRIC EXPERIENCE

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Background and Aims:: Treatment with botulinum toxin A (BoNT-A) is the first-line therapy of cervical dystonia (CD). The aim of this study is to evaluate long-term efficacy and tolerability of BoNT-A and treatment efficacy predictors in a CD monocentric cohort, over two decades.

Methods:: We retrospectively analyzed treatment data of 178 consecutive CD patients in our outpatient clinic, treated with BoNT-A according to clinical practice, from July 2002 to March 2021. Dosage, treatment pattern, time between visits and follow-up duration were adopted as explanatory variables. Variations in objective (TWSTRS) and subjective scales (GTS), as well as duration of the benefit and side effects, were used as outcome measures to assess treatment efficacy.

Results:: We analyzed 4039 treatment sessions, with a median follow-up of 5 years [IQR: 1-11]. A end-dose mitigation in severity from baseline was observable in the majority of cases (median ΔTWSTRS: -10[IQR: -19; -1]), no development of resistance was reported. Instead, we observed a tendency in stabilizing the dosage after the first years of treatment. None of the explanatory variables emerged as a clear predictor for efficacy, reflecting the heterogeneity in disease courses. Side effects included mild dysphagia(8%), muscle weakness(1%), and local pain(2%), the latter correlating with infiltrations of the splenius(p=0.01). Frequent reasons for therapy discontinuation included treatment failure(12%) and persistent benefits(8%).

Conclusions:: BoNT-A treatment is an effective therapy for CD, even over many years. Due to the intrinsic heterogeneity of the disease, a deterministic predictor of treatment response is yet to be found in the out-patient setting. Treatments need to be patient-tailored, majorly relying on physician experience.
CHRISTIANSON SYNDROME MANIFESTED AS ATYPICAL PARKINSONISM: A CASE REPORT

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Background and Aims:: Christianson syndrome (CS) is an X-linked disorder characterized by cognitive dysfunction, behavioral abnormalities and neurologic findings such as ataxia, abnormal eye movement, feeding difficulties, lack of facial expression, hyperkinesia and seizures. Here, we describe a case of a male with CS with severe parkinsonism.

Methods:: Case report.

Results:: A 41 year-old man with intellectual disability consulted for slowness of movements, progressive cognitive decline, sleep disturbances and hypersalivation with swallowing problems. The medical exam showed severe bradykinesia, hypomimia, generalized dystonia, left asymmetric tremor and supranuclear gaze palsy. In the personal medical history, the mother suffered from genetic Parkinson (LRKK2). Treatment with carbidopa/levodopa did not improve the symptoms. Therefore, a diagnosis of atypical parkinsonism was made. Blood tests (including TSH, CK and ceruloplasmin) and Brain-MRI were unremarkable. DATSCAN showed neuronal loss via the presynaptic nigrostriatal with greater involvement of the right striatum. Extensive genetic study (including LRRK2, PARK-1-3-6-7, SCA 1-2-3-7-8-17, DYT-5, FXTAS, Nieman-Pick and Huntington) was negative. Whole-exome sequencing showed a hemizygous c.767GA (p.S256N) missense pathogenic variant in the SLC9A6 gen on the X-chromosome associated with Christianson syndrome. A genetic study of the mother and two sisters showed the same pathogenic variant in the SLC9A6 gen (female carriers).

Conclusions:: CS may present with severe bradykinesia and supranuclear gaze palsy, mimicking an atypical parkinsonism syndrome. Neurologist should be aware that, although hyperkinesia is a frequent symptom, bradykinesia may be present difficulting the diagnosis of CS. Therefore, we highly recommend performing an extensive genetic testing aimed for genetic counseling.
SEX DIFFERENCES IN CORTICAL HEMODYNAMIC RESPONSE TO LEVODOPA IN PARKINSON’S DISEASE PATIENTS: A FUNCTIONAL NIRS STUDY

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Background and Aims:: The aim of this study was to investigate sex differences in hemodynamic response of the cortical motor system after levodopa intake, in patients affected by Parkinson’s disease (PD) with levodopa-induced dyskinesias (LID), by means of functional near-infrared spectroscopy (fNIRS).

Methods:: Patients fulfilling UK Brain Bank criteria for PD, referring to the Movement Disorders Center of the University “Magna Graecia” of Catanzaro, were consecutively recruited. Main inclusion criteria were a) presence of LID; b) duration of levodopa treatment greater than 6 months; c) stable dosages of levodopa treatment for at least 4 weeks. All patients were evaluated by means of motor UPDRS and AIMS scale at baseline (T0), after 1 (T1), and 2 (T2) hours from levodopa intake. NIRS study was performed at the same time-points.

Results:: Nine PD patients with LID were included. Four were females (age: 60.83 ± 4.17 years, mean ± SD) and five were males (age: 61.00 ± 14.00 years; p=0.978). In NIRS study, in men a gradual increase in oxygenated-hemoglobin (HbO) concentrations of motor cortex was observed at T1 and T2, in comparison to T0. By contrast, women showed a reduction in HbO concentrations at T1 in comparison to T0, followed by a return to baseline hemodynamic activation levels after 2 hours from levodopa intake.

Conclusions:: Our preliminary results of this fNIRS study showed a significant difference in the motor cortical haemodynamic responses to levodopa intake in male and female patients with PD and dyskinesias. Further studies on sex-disaggregated data to interpret differential cortical activation in PD are needed.
THE HUMAN M-OPIOID RECEPTOR GENES POLYMORPHISM IS NOT ASSOCIATED WITH LEVODOPA-INDUCED DYSKINESIA DEVELOPMENT IN RUSSIAN PATIENTS WITH PARKINSON’S DISEASE

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Background and Aims:: Levodopa-induced dyskinesia (LID) occurs in the vast majority of PD patients after several years of levodopa therapy. But the time of their development and severity differ in different individuals - it depends on pharmacological factors and individual characteristics. Opioid systems can also be involved in the development of LID - opioids are co-transmitters in both the direct and indirect pathways of the basal ganglia.

Methods:: Our clinical study was included 631 sporadic PD patients from the Republic of Bashkortostan. Patients used levodopa for not less than 1 year. The analysis of polymorphism rs1799971 - the human μ-opioid receptor genes (OPRM1) SNP was performed. Dyskinesia was assessed using of MDS-UPDRS scale (parts IV). Were taken into account sex, age of onset PD, duration of levodopa therapy, and a total daily dose of antiparkinsonian medication (levodopa equivalent dosage, LED). The SPSS software was used for statistical analysis. Linear regression and one-way analysis of variance (ANOVA) were used. A P-value<0.05 was considered statistically significant.

Results:: Thus, the presence of all motor levodopa-induced complications was assessed in 212 PD patients. Dyskinesias were identified in 106 (50.00%) patients (67 female, 39 male). There is no association between the rs1799971 genotype and LID development.

Conclusions:: Studies using positron emission tomography in patients with LID have shown a lower binding of opioid ligands in the striatum and thalamus. Other studies have found that this SNP of the OPRM1 gene affects the timing of dyskinesia development in PD patients. Further research is needed. The work was supported by RFBR grant #19-015-00331
THE PREVELANCE OF RESTLESS LEG SYNDROME IN ULAANBAATAR CITY’S ADULTS

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Background and Aims:: Introduction: The most of people with restless leg syndrome (RLS) rarely seek medical attention, usually through a screening. Accordingly, it has a significant impact on the quality of life. Health and socioeconomic impact of sleep related disorders reveals that the prevalence of RLS is high in the population and it has effect on the quality of life. Objective: To determine the prevalence of restless syndrome in Ulaanbaatar.

Methods:: A total of 826 adults aged 18-65 years were included and screened by a questionnaire.

Results:: 6.7% (n=55) of the people had a RLS. There was a statistically significant difference in mean age and sex between the demographics of those who were diagnosed and those who were not (p <0.01). 5.9% of men (n = 12) and 7.2% of women (n = 43) were found to have RLS, which is statistically more likely to frequent in women (p <0.01). In terms of age, RLS is more prevalent in the elderly (35-55 years old).

Conclusions:: Conclusion: The prevalence of RLS in Ulaanbaatar is 6.7% which is higher in women and in both sexes aged 35-55 and older.
THE EFFECTS OF LEVODOPA CHALLENGE TEST ON EYE MOVEMENTS IN PARKINSON’S DISEASE: INSIGHTS FROM A DE NOVO COHORT.

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Background and Aims:: Clinical eye movement quantitative assessment represents a promising non-invasive tool to investigate both pathophysiology and clinical aspects of neurodegenerative disorders. In Parkinson’s disease (PD), eye movements abnormalities involving both saccadic and smooth pursuit movements were described and investigations about the effects of antiparkinsonian drugs on eye motility provided conflicting evidences. Notably, only few studies with small sample sizes assessed Levodopa (LD) effects on a drug-naïve population through a standardized Levodopa Challenge Test (LCT). Moreover, few data are available about vertical eye movements after LD administration while nothing is known about fixation parameters. Here we aimed to widely investigate eye motility effects of LCT in a de novo PD population.

Methods:: De novo patients fulfilling MDS diagnostic criteria for clinically-probable PD were enrolled. Eye movement were recorded by Eyelink 1000 Plus. Horizontal and vertical visually-guided saccades, horizontal and vertical smooth pursuit movements (SPM) and fixation parameters were assessed at baseline and after 2 hours from the administration of Levodopa/Carbidopa 250/25 mg.

Results:: Forty de novo PD patients were enrolled [23 Men (57.5%); age (mean±SD) 64.5±6.9 years; disease duration 1.7±1.1 years; baseline UPDRS-ME 25.8±8.3; peak UPDRS-ME 21.3±8.3]. We found an improvement in saccadic velocities and accuracy as well as reduced horizontal latencies after LD administration. Moreover, a reduction of saccadic inclusion rate in fixation tasks and an increased vertical SPM gain were demonstrated.

Conclusions:: Our findings from a de novo population partially confirmed literature evidences, enlighting interesting insights about acute LD effects on SPM, fixation parameters and saccadic latencies.
ROLE OF APOLIPOPROTEIN E IN THE CLINICAL PROFILE OF ATYPICAL PARKINSONIAN SYNDROMES

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Background and Aims:: Atypical parkinsonian syndromes (APS) encompass a spectrum of neurodegenerative diseases including dementia with Lewy bodies (DLB), Progressive Supranuclear Palsy (PSP), Multiple System Atrophy (MSA) and corticobasal syndrome (CBS). The effects of the ApoE gene on the clinical features of these diseases are controversial and understudied in several populations. Our aim was to explore the influence of ApoE genotype on clinical features across the different APS subgroups in a Tunisian population.

Methods:: In a retrospective cross-sectional descriptive study in the department of Neurology of Razi Hospital, we included clinically-diagnosed APS patients genotyped for ApoE. The associations between clinical, neuropsychological data and ApoE genotype were analyzed.

Results:: A total of 328 APS patients were included: 184 DLB, 58 PSP, 49 MSA and 37 CBS. Executive dysfunction was more pronounced among patients with ApoE ε4 allele, specifically among DLB and less observed in MSA cases. Memory disorders were also associated to ApoE ε4 allele and more frequent among DLB and PSP carriers. Conversely, ApoE ε4 carrying status was not associated with gender, age of disease onset, nor parkinsonism onset.

Conclusions:: Our findings suggested a role of ApoE ε4 in defining a more altered cognitive phenotype in APS patients, especially in DLB carriers.
OPICAPONE-INDUCED REVERSIBLE MYOPATHY IN A PATIENT WITH ADVANCED PARKINSON’S DISEASE AND FAMILIAL HYPERCKEMIA

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Background and Aims:: Opicapone (OPC) is a third-generation catechol-O-methyltransferase inhibitor, which has proven effective in Parkinson disease (PD) patients. Among common adverse events, several studies have reported OPC induced mild and reversible increase of blood creatine phosphokinase (CK). We present a case report of a 70-year-old man with PD admitted to our department with bilateral drooping eyelids, progressive difficulties in climbing stairs and severe increases of blood CK levels after addition of OPC to levodopa treatment.

Methods:: The patient was not taking drugs for other medical conditions and denied trauma. The serum CK level, after rest, was increased (CK = 9329 U/l, normal range: 0–175 U/l) as well as LDH and myoglobin. The other laboratory hematology and biochemistry tests, chest radiography, abdomen echography, ECG and echocardiography were all normal. EMG with quantitative motor unit potential (MUP) analysis showed signs of mild myopathic damage.

Results:: After discontinuing OPC administration, the patient completely recovered in 5 weeks. One month after full recovery, CK value was 280 U/l. An EMG, 3 months after recovery, showed a normalization of the PUM analysis. Additional interrogation of the medical history revealed that the patient had been occasionally suffering cramps and myalgia after vigorous muscle exercise. Thus, we extended laboratory studies to all available adult family members, and routine serum chemistry revealed an elevated CK level at rest in three relatives.

Conclusions:: CK dosage before and during OPC therapy in PD patients is recommendable. A family history positive for hyperCKemia in PD patients might be a risk factor for marked OPC-related CK increase.
COGNITIVE PROFILES BASED ON MRI VENTRICULAR SIZE MEASUREMENTS IN PATIENTS WITH IDIOPATHIC NORMAL PRESSURE HYDROCEPHALUS AND ALZHEIMER DISEASE. IMPLICATIONS FOR A DIAGNOSTIC APPROACH

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Background and Aims:: To evaluate the association between ventricular size measurements and cognitive performances in patients with cognitive complaints validating measurements with confirmed clinical diagnosis.

Methods:: We identified patients with cognitive impairment who underwent both standardized neuropsychological evaluation and MRI study demonstrating cerebral ventricular enlargement. Evans’ Index (EI), Temporal Ratio (TR) and Parieto-Occipital Ratio (POR) were calculated based on neuroimaging. After the diagnostic workup, a diagnosis of idiopathic Normal Pressure Hydrocephalus (iNPH) or Alzheimer Disease (AD) was made. Considering discriminating cut-off values of each index, cognitive performances between patients were compared. Sensitivity and specificity of computed indices in discriminating iNPH from AD were estimated.

Results:: Fifty-two patients were identified. Regardless clinical diagnosis, 27 patients with normal EI had statistically-significant lower score on Rey Auditory Verbal Learning Test (RAVLT), both immediate (p=0.22) and delayed recall (p<0.001) as compared to 25 patients with abnormal EI. Thirteen patients with normal TR had statistically-significant lower score at the RAVLT-delayed recall (p<0.027) as compared to 38 patients with abnormal TR. No statistically-significant differences in cognitive performances were found between identified two groups on POR (8 pathological vs 44 normal). Twenty-six patients were diagnosed as iNPH (20 probable iNPH, 6 possible iNPH). Twenty-six patients received a diagnosed of probable AD. Sensitivity and specificity of MRI measures in differentiating iNPH vs AD were respectively: 84%(95%CI:65.1-95.6) and 87%(95%CI:60.6-93.4) for EI; 100%(95%CI:86.3-100) and 50%(95%CI:29.9-70) for TR; 30.7%(95%CI:14.3-51.8) and 100%(95%CI:86.7-100) for POR.

Conclusions:: EI and TR measures differentiated amnestic patterns among study subjects. EI demonstrated the best accuracy in distinguish iNPH from AD.
**Background and Aims::** Ataxia, defined as loss of balance and coordination, is a clinical symptom of a heterogeneous group of diseases with acquired, inherited, or sporadic etiology. The disorder is caused by dysfunction of the cerebellum, spinal cord, brainstem, vestibular nuclei, thalamic nuclei, cerebral white matter, cortex (frontal), or peripheral sensory nerves. Toxic-metabolic, immune-mediated, paraneoplastic, degenerative, infectious, hereditary, or functional disorders might lead to sporadic ataxia: a neurological condition affecting adults with negative family history.

**Methods::** A 39-year-old woman had been presented with a two-year history of sudden-onset tremor and rapid progressive ataxia. Her family history was unremarkable, and there was no history of consanguinity. On in-depth examination, she had no nystagmus, normal external-eye-movements and speech, mild postural wrist flexion-extension tremor (right> left), ataxic gait with severe difficulties on standing, and tandem walk. Her writing did not suggest any tremor-dystonic features. Brain MRI showed normal cerebral and cerebellar parenchyma, SPECT DAT scan excluded dopamine-deficit, SEP, EMG, as well as blood and cerebrospinal fluid exams (antibodies against the central nervous system, thyroid function, rheumatologic antibodies, gluten sensitivity, vitamin E, vitamin B12, ceruloplasmin, serum and urine copper, alpha-fetoprotein, neurotropic viruses), were normal.

**Results::** The patient followed a rehabilitation program, improving her gait and balance. At follow-up, she reported marriage breakdowns, and we detected variability, distractibility, entrainability, and suggestibility on her tremor and standing imbalance. Functional ataxia-tremor disorder was diagnosed.

**Conclusions::** Adult-onset ataxia should be first investigated for organic etiologies; however, careful anamnesis and detail neurological examination is mandatory not to miss functional disorder.
Background and Aims:: Mutations in the cytoplasmic dynein 1 heavy chain 1 (DYNC1H1) gene are associated with autosomal dominant lower extremity-predominant spinal muscular atrophy, neuromuscular and neurodevelopmental disorders and hereditary spastic paraplegia. We report a case of adult-onset Parkinson’s disease associated to a mutation of DYNC1H1 gene.

Methods:: Case presentation and literature review.

Results:: A 58-years-old caucasian man developed progressive motor slowing in the right limbs. His medical history revealed diabetes mellitus and hypertension. His brother suffered from intellectual disability, epilepsy and interatrial septum aneurysm. The patient presented strabismus, antiverse nares and fleshy lips; occipitofrontal circumference measured 58.5 cm (>97°c). He showed parkinsonism predominantly in the right limbs. Brain MRI scan displayed corpus callosum hypoplasia. DaTscan SPECT imaging showed decreased uptake in the striatum bilaterally. The neuropsychological evaluation revealed a globally poor cognitive performance at the frontal battery and cognitive slowing. Routine laboratory work-up was unremarkable. Poor response to L-dopa challenge test and long-term L-dopa therapy was observed. Molecular analysis for FMR1 gene and array-CGH were normal. Next generation sequencing of customized panel targeting 63 genes associated with neurodevelopmental disorders and macrocephaly was performed, detecting c.13783C>T (p.Gln4595Ter) heterozygous variant in DYNC1H1 gene.

Conclusions:: Unlike a previous described case with DYNC1H1 mutation and parkinsonism, our patient was unresponsive to the dopaminergic therapy and showed corpus callosum hypoplasia. Further studies are required to define the effect of this mutation and its possible causative role in parkinsonism. 1 Szczaluba, (2018), A de novo loss-of-function DYNC1H1 mutation in a patient with parkinsonian features and a favourable response to levodopa. Clin Genet.
CEREBROSPINAL FLUID A/T/(N) PROFILE AND MILD COGNITIVE IMPAIRMENT IN PARKINSON’S DISEASE

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Background and Aims:: In synucleinopathies, the presence of an underlying Alzheimer’s disease (AD) pathology can be involved in cognitive decline. Cerebrospinal fluid (CSF) profile consistent with amyloidosis, as well as CSF AD signature are sometimes reported in Parkinson’s disease (PD) with dementia. Additionally, decreased CSF Aβ42 levels predict earlier appearance of cognitive decline in PD. However, contradictory results are available for CSF AD biomarkers in PD patients with mild cognitive impairment (PD-MCI). Our aim was to assess potential correlation between CSF AD biomarkers and PD-MCI.

Methods:: CSF samples were collected from 50 cognitively unimpaired PD and 48 PD-MCI patients. We measured CSF Aβ42/Aβ40 ratio, p-tau and t-tau levels as biomarkers of amyloidosis (A), tauopathy (T) and neurodegeneration (N), respectively. A/T/(N) profile was considered for each patient.

Results:: No significant differences were found between PD and PD-MCI groups in terms of CSF Aβ42/Aβ40 ratio, p-tau and t-tau levels, that were in the normal range for most patients. Accordingly, the A-/T-/N- profile was the most frequent in both PD and PD-MCI groups, with low frequencies of A+ (10% and 12% respectively), T+ (4% and 6% respectively) and N+ (16% and 12% respectively), without showing differences.

Conclusions:: The CSF A/T/(N) profile of PD-MCI patients did not differ from cognitively unimpaired PD patients, being the A-/T-/N- the most frequent pattern in both groups. Thus, MCI in PD is not necessarily associated with amyloidosis or AD-pathology, but rather it is a heterogeneous entity in which other pathologies might be involved.
SHORT- AND LONG-TERM MOTOR OUTCOME OF STN-DBS IN PARKINSON'S DISEASE: FOCUS ON GENDER DIFFERENCES.

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Background and Aims:: STN-DBS is an established treatment for Parkinson’s Disease with motor fluctuations and dyskinesias but studies on the long-term outcome are still scarce. In this study, we describe the long-term motor outcome of STN-DBS in a cohort of patients consecutively treated in our centre, with a focus on the possible differences associated with gender.

Methods:: We reviewed all patient charts from our electronic database and retrospectively collected demographical and clinical data at baseline and at three follow-up visits: 1 year, 5 years and 10 years. 107 patients were included. 41 reached 10-years follow-up.

Results:: We found and long-lasting effect of DBS on motor complications, despite a progressive worsening of motor performances in the ON medication condition. Females showed a trend towards worsening in bradykinesia already at 1-year follow-up and possible poorer scores in non-dopaminergic features at 10-years follow-up. Levodopa Equivalent Daily Dose (LEDD) was significantly reduced after surgery however, while in males remained significantly lower than baseline, in females LEDD returned at baseline values at 10-years follow-up. Males showed a sustained effect on dyskinesias but this benefit was less clear in females and the Total electrical energy delivered by STN-DBS was consistently lower in females compared to males. The profile of Adverse Events did not appear to be influenced by gender.

Conclusions:: Our data suggest that there are no major differences on the motor effect of STN-DBS between males and females. However, there may be some slight differences that should be specifically investigated in the future and may influence therapeutic decisions.
PERAMПANEL INHIBITS Α-SYNUCtEIN TRANSMISSIΟΝ IN PΑRKΙНSON’S DISEASE MODELS

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Background and Aims:: The intercellular transmission of pathogenic proteins plays a key role in the clinicopathological progression of neurodegenerative diseases. Previous studies have demonstrated that this uptake and release process is regulated by neuronal activity. The aim of this study is to examine the effect of perampanel, an antiepileptic drug, on α-synuclein transmission in cultured cells and mouse models of Parkinson’s disease.

Methods:: Mouse primary hippocampal neurons were transduced with α-synuclein preformed fibrils to examine the effect of perampanel on the development of α-synuclein pathology and its mechanisms of action. An α-synuclein preformed fibrils-injected mouse model was used to validate the effect of oral administration of perampanel on the formation of α-synuclein pathology in vivo.

Results:: Perampanel inhibited the development of α-synuclein pathology in mouse hippocampal neurons transduced with α-synuclein preformed fibrils. Interestingly, perampanel blocked the neuronal uptake of α-synuclein preformed fibrils by inhibiting macropinocytosis in a neuronal activity-dependent manner. We confirmed that oral administration of perampanel ameliorated the development of α-synuclein pathology in wild-type mice inoculated with α-synuclein preformed fibrils.

Conclusions:: Targeting neuronal activity with perampanel could represent a new therapeutic strategy for Parkinson’s disease.
SUSTAINED IMPROVEMENTS IN MOTOR AND NON-MOTOR SYMPTOMS IN ADVANCED PARKINSON’S DISEASE PATIENTS TREATED WITH CARBIDOPA LEVODOPA ENTERAL SUSPENSION IN A ‘REAL-WORLD’ STUDY

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Background and Aims:: We evaluate effect of levodopa–carbidopa intestinal gel(LCIG, carbidopa-levodopa enteral suspension[CLES] in USA)on motor and nonmotor symptoms in a multi-country observational study in advanced Parkinson’s disease (PD) patients treated with LCIG in routine clinical practice.

Methods:: DUOGLOBE is a prospective multinational observational study (including US sites) of LCIG/CLES naïve patients treated in routine clinical practice with 3-years follow-up planned (NCT02611713). Assessments included “Off” time, Unified Dyskinesia Rating Scale (UDysRS), Non-Motor Symptoms Scale (NMSS), sleep symptoms (PD Sleep Scale-2, PDSS-2), Quality of Life (8-item PD questionnaire, PDQ-8), and Serious Adverse Events (SAEs). Interim outcomes from baseline up to month (M) 24 are presented.

Results:: In this interim analysis, 196 patients were included (62% male, 78% ≥65 years old; 51% ≥10 years’ PD duration). Mean (SD) LCIG treatment duration was 711 (368) days with a median daily LCIG/CLES infusion of 16.0 h/d. Significant improvements (mean change from baseline to M24) were observed in “Off” time (~3.7 h/d; 95% CI -4.3 to -3.1; p<.001), UDysRS total scores (~7.9; 95% CI -12.5 to -3.2; p<.001), NMSS total scores (~22.2; 95% CI -30.7 to -13.7; p<.001), PDSS-2 total score (~5.8; 95% CI -8.2 to -3.3; p<.001), and QoL (~5.8; 95% CI -10.0 to -1.5; p=0.009). Overall, 52% of patients experienced SAEs. 23% (n=45) of patients discontinued the study due to AEs as primary reason.

Conclusions:: This interim analysis shows sustained real-world long-term improvements with LCIG/CLES in routine clinical practice on motor and non-motor symptoms in advanced PD patients. Safety was consistent with the established LCIG/CLES profile.
Background and Aims:: Deep brain stimulation (DBS) is an effective treatment in patients with movement disorders (MD). DBS program was adapted in every country differently and patients’ visits became mostly via telemedicine in this pandemic time.

Methods:: We present organizing problems and management of DBS in Croatia and compare outcomes of DBS implanted for MD in year 2019 and 2020 by using standard scales for PD, essential tremor and dystonia.

Results:: When we compared implanted patients, we had more in 2019 (60/20). It was hard to organize operation due to transition UHC Dubrava (the only DBS center in Croatia) in National COVID 19 hospital and operation had to be carefully planed in other UHC hospitals between shifts of DBS team’s members in COVID-19 hospital and free operations rooms. The motor symptoms’ outcomes in PD, dystonia and essential tremor were without significant difference in both years, but anxiety was bigger in 2020. Transient hallucinations were slightly more often in 2020 (2/60 vrs. 3/20). We had 3 previously operated patients with discharged battery and worsening of symptoms due to their hesitation to report that to our DBS team in time.

Conclusions:: This COVID 19 pandemic presents unique challenge for management of DBS in MD. A lot of centers must deal with quick moving and adjustments of DBS program to other hospitals and invest more effort in maintaining it. Neuropsychiatric symptoms had to be monitored all the time, especially in this pandemic time.
INVESTIGATION OF OROPHARYNGEAL SWALLOWING AND SWALLOWING-BREATHEING COORDINATION IN PATIENTS WITH PARKINSONIAN SYNDROMES. AN ELECTROKINESIOGRAPHIC APPROACH.

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Background and Aims:: Multiple system atrophy (MSA) is a neurodegenerative disorder characterized by dysautonomia in combination with parkinsonian and cerebellar signs. Dysphagia typically occurs in the early stages of the disease also representing a life-threatening condition that is at least in part responsible for the poorer prognosis with respect to Parkinson disease (PD). The pathophysiology of dysphagia in MSA is still poor understood. Aim: To investigate with an electrokinesiographic approach abnormality of swallowing and coordination between swallowing and breathing in different MSA phenotypes in comparison with PD and age-matched normal subjects.

Methods:: We recruited 45 patients with MSA (35 with parkinsonian, MSA-P, and 14 with cerebellar phenotype, MSA-C), 20 patients with PD and 15 healthy subjects. The electrokinesiographic study of swallowing consisted in a combined evaluation of different electrophysiological and mechanical aspects of oropharyngeal swallowing also including recording of nasal airflow during swallowing to evaluate the physiological swallowing respiratory pause.

Results:: Oropharyngeal alterations similar to that of PD were observed in patients with MSA (oropharyngeal bradykinesia, piecemeal deglutition, posterior spillage, incomplete relaxation of the cricopharyngeal muscle). Additional abnormalities compatible with incoordination between the oral and pharyngeal phase of swallowing and between swallowing and breathing were observed in patients with MSA-C.

Conclusions:: The pathophysiology of dysphagia may differ between different MSA phenotypes. In particular, an additional cerebellar dysfunction could contribute to dysphagia in MSA-C.
PROGRESSIVE SUPRANUCLEAR PALSY: CLINICAL, INSTRUMENTAL AND NEUROPSYCHOLOGICAL EVALUATION OF A CASE IN THE PRESYMPTOMATIC PHASE

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Background and Aims:: Atypical parkinsonisms are a group of sporadic neurodegenerative diseases. Atypical Parkinsonisms include Multiple System Atrophy (MSA), Progressive Supranuclear Palsy, Cortico-Basal Syndrome and Lewy Body Dementia. The present study aims to describe a very interesting clinical case while no clinical signs are presented, characteristic signs emerge from instrumental examination. PSP is characterized by early postural instability, vertical gaze paralysis, parkinsonism, pseudobulbar symptoms, absent response to Levodopa.

Methods:: We describe the case of a 50-year-old man who presented the onset of a motor epileptic seizure. A CT scan was performed on the patient that showed no pathological data. A brain MRI was also performed, showing atrophy of the midbrain with penguin and mickey mouse sign. Brain PET scan showed diffuse inhomogeneity of radiopharmaceutical fixation. The neuropsychological evaluation has integrated several components.

Results:: The results of the neuropsychological evaluation are in the table
Conclusions: Neuropsychological examination show deficits in episodic memory anterograde for both verbal and non-verbal material, which are associated with defects of consolidation; deficits in working memory and executive functions to which are associated reduced verbal fluency and moderate deflection of mood. Nevertheless, the patient has good communication skills and verbal comprehension, praxic-constructive and fair logical reasoning skills. The patient's neuropsychological profile appears congruent with an impairment of diencephalic, temporomental, and fronto-subcortical structures. Our patient on the
The phonemic verbal fluency test is able to produce 6 words in 1 minute. It has been reported that patients who produce fewer than 7 words in a minute are much more likely to have PSP than PD.
LOW CONCENTRATIONS OF BILIRUBIN PROTECT FROM DOPAMINERGIC NEURON LOSS IN AN EX VIVO MODEL OF PARKINSON DISEASE

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Background and Aims:: Disease-modifying therapy for Parkinson’s disease (PD) is still an unmet medical need. Hence, we investigated the protective effects of unconjugated bilirubin (UCB) in an ex vivo PD model and identified the protective UCB concentrations threshold.

Methods:: A slow-progressing ex vivo PD model obtained by exposing organotypic brain cultures (OBCs) of substantia nigra from 5 days old Wistar rat to low doses of rotenone, has been co-challenged for 24 hours with a range concentration (0.5μM to 4μM) of UCB. Immunofluorescence was used to counts the number of DOPAn. RT-qPCR was used to monitor the early alteration of genes involved in the DOPAn demise (oxidative stress: Srnx1: sulfiredoxin 1; inflammation: Tnfα: tumor necrosis α, Il6: interleukin 6, Cox2: cyclo-oxygenase 2; and neurotrophic genes: Bdnf: brain-derived neurotrophic factor).

Results:: The DOPAn number was significantly reduced in Rot-treated OBCs (-35%, p < 0.01), associated with significant induction of all tested genes (all p<0.05). A full reversal of DOPAn number was obtained with 0.5 μM and 1 μM UCB challenging (both p<0.05 vs. Rot). 0.5μM UCB reverted Tnfα expression (p<0.01 vs. Rot). Meanwhile, 1μM UCB restored the expression of Tnfα, Il6, and Bdnf (p<0.05, p<0.01, and p<0.05, respectively). 2μM UCB decreased the expression of Il6 (p<0.01), while 4μM UCB increased the mRNA level of all the selected markers above the expression in Rot challenged slices.

Conclusions:: Low concentrations of UCB have a protective effect on the PD model as anti-inflammatory agents at 0.5μM and 1μM
IMPACT OF MEDIUM-CHAIN SATURATED FATTY ACIDS ON MOTOR FUNCTION IN PATIENTS WITH PARKINSON’S DISEASE

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Background and Aims:: Medium-chain saturated fatty acids (Octanoic acid (C8:0) and Decanoic acid (C10:0)) are found in high levels in coconut oil and palm kernel oil, commonly used in processed foods in the United States. They have reportedly positive effects on neuronal function in epilepsy and on cognition in Alzheimer’s Disease. However, negative effects have been described in vascular diseases (such as stroke). Less is known about the impact of these fatty acids in Parkinson’s Disease (PD). This study explored the association between their dietary intake and motor function in PD.

Methods:: We prospectively enrolled patients from Comprehensive PD Clinic at the University of Nebraska Medical Center and completed Harvard food frequency questionnaire (FFQ) for quantification of dietary intake along with baseline assessments. Linear regression was used to evaluate the association between Octanoic and Decanoic acid intake and the Unified Parkinson Disease Rating Scale (UPDRS) motor score, with adjustment for relevant confounders.

Results:: 117 participants with Parkinson’s Disease were included in the final analysis. Mean Octanoic and Decanoic acid intakes were 0.2 and 0.4 g/day, respectively. A significant association between dietary intake and UPDRS motor score was observed for Octanoic acid ($\beta = 0.21$, $p= 0.03$) while Decanoic acid approached significance ($\beta = 0.17$, $p = 0.07$).

Conclusions:: Increased intakes of Medium Chain Saturated fatty acids may adversely affect motor function in subjects with Parkinson’s Disease, requiring further exploration.
THERAPEUTIC POTENTIAL OF INHIBITION OF FORMYL PEPTIDE RECEPTOR SIGNALING IN PARKINSON’S DISEASE

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Background and Aims:: Microglia-mediated neuroinflammation is one of the major pathogenesis of Parkinson’s Disease (PD). Evidences suggest that formyl peptide receptors (FPRs), a family of transmembrane chemoattractant receptors, are implicated in the activation of microglia into the pro-inflammatory subtype. The present study investigated the mechanism and neuroprotective effect of dipeptide N-(N-benzoyl-L-tryptophanyl)-D-phenylanlanine methyl ester (HCH6-1), an inhibitor of FPR, in a neuroinflammation model of PD.

Methods:: The neuroinflammatory in vitro model was established by using co-culture system consisting of neuronal SH-SY5Y cells and microglial EOC-20 cells. Cells were then subjected to either Lipopolysaccharides (LPS) stimulation only or combination of HCH6-1 pre-treatment and LPS stimulation.

Results:: LPS stimulation resulted in increased cell apoptosis, oxidative stress, ER stress, and inflammatory reactions. HCH6-1 pre-treatment attenuated LPS-induced apoptotic cell death in a dose-dependent manner as measured by cell viability and TUNEL assay. Subsequent immunofluorescence assay of intracellular reactive oxygen species (ROS) and malondialdehyde (MDA) lipid peroxidation assay revealed that HCH6-1 reduced LPS-induced increase of oxidative stress. Furthermore, western blot analysis demonstrated that HCH6-1 pre-treatment decreased the expression levels of both ER stress related protein markers, GFP78, ATF6, activated caspase-12, and inflammatory protein markers, AIM2, NLRP3, ACS/TMS1, TNF-α, IL-1β, activated caspase-1.

Conclusions:: The results showed that HCH6-1 is effective to reduce apoptotic cell death and attenuate oxidative stress, ER stress, and inflammation in LPS-induced neuroinflammation model of PD. FPR1 blocking might be promising to develop neuroprotective therapy for PD.
EFFICACY AND SAFETY OF FOSLEVODOPA/FOSCARBIDOPA VERSUS ORAL CARBIDOPA/LEVODOPA IN ADVANCED PARKINSON'S DISEASE PATIENTS: DESIGN OF A PHASE 3, RANDOMIZED, DOUBLE-BLIND, DOUBLE-DUMMY, ACTIVE CONTROLLED 12-WEEK TRIAL

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Background and Aims:: We compare efficacy and safety of 12-week continuous subcutaneous infusion (CSCI) of foslevodopa/foscarbidopa, a new soluble formulation of carbidopa (CD) and levodopa (LD) prodrugs formally known as ABBV-951a, versus oral CD/LD for the treatment of motor fluctuations in advanced Parkinson's disease (PD) patients.

Methods:: This phase 3, randomized, double-blind, double-dummy, parallel-group, active-controlled, multicenter study includes patients (≥30 years) whose motor symptoms are no longer adequately controlled by their current therapy and experience a minimum daily average of 2.5h of “Off” time per day (with a minimum of 2.0h each day). The study is comprised of a screening period, and an oral CD/LD stabilization period, followed by randomization into the 12-week double-blind treatment period. Patients will receive either 24-hour/day CSCI of foslevodopa/foscarbidopa plus oral placebo or 24-hour/day CSCI of placebo solution plus oral CD/LD. Assessments include the change from baseline to Week 12 in "On" and “Off” times from PD Diaries, MDS-UPDRS scores, quality of life, sleep symptoms, and PD symptoms measured using a wearable device. Local and systemic safety and tolerability will be assessed using the Infusion Site Evaluation Scale and adverse event monitoring.

Results:: This study will enroll approximately 130 advanced PD patients from an estimated 80 sites in the United States and Australia (clinicaltrials.gov ID: NCT04380142).

Conclusions:: This study will provide important data on the safety and efficacy of foslevodopa/foscarbidopa, a potentially new advanced treatment option, delivered 24-hour/day via CSCI versus oral CD/LD in advanced PD patients.
FOSLEVODOPA/FOSCARBIDOPA SUBCUTANEOUS INFUSION MAINTAINS EQUIVALENT LEVODOPA EXPOSURE TO LEVODOPA-CARBIDOPA INTESTINAL GEL DELIVERED TO THE JEJUNUM

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Background and Aims:: Levodopa-Carbidopa Intestinal Gel (LCIG) 16-hour infusion offers superior symptomatic control than oral levodopa/carbidopa in patients with advanced Parkinson's disease (aPD); however, it requires percutaneous endoscopic gastrostomy tube placement. Foslevodopa/foscarbidopa is an investigational drug being developed for treatment of aPD providing 24-hour therapeutic levels of levodopa following subcutaneous (SC) delivery. We characterize levodopa pharmacokinetics (PK) following foslevodopa/foscarbidopa SC infusion and LCIG jejunal infusion in healthy volunteers.

Methods:: This open-label, 2-way crossover study randomized, 20 healthy volunteers. In each period, subjects received either 24-hour foslevodopa/foscarbidopa SC infusion to the abdomen or 16-hour LCIG infusion to the jejunum through a nasojejunal tube followed by two separate nighttime oral levodopa/carbidopa (LD/CD) doses. Serial blood samples were collected to assay for levodopa concentrations. Equivalent levodopa exposure was predefined as the ratio (ABBV-951/LCIG) and 90% confidence interval of exposure parameters between 0.8 and 1.25. Safety and tolerability were assessed throughout.

Results:: Foslevodopa/foscarbidopa SC infusion provided equivalent levodopa levels to LCIG infusion over the 16-hour interval and maintained those levels throughout the nighttime. Exposure difference between the two regimens was less than 8% and well contained within defined equivalence range. Based on PK predictions, overall levodopa exposures over 24 hours also showed equivalence between foslevodopa/foscarbidopa SC infusion and LCIG. Both regimens were generally safe and well tolerated in healthy volunteers. All adverse events considered to be “possibly related” to study drug were mild and did not lead to discontinuation from the study.

Conclusions:: Foslevodopa/foscarbidopa SC infusion delivers equivalent levodopa exposure to LCIG infusion with and without nighttime oral LD/CD dosing.
EVALUATION OF THE CHANGING CLINICAL OUTCOMES AND DISEASE BURDEN IN ADVANCED PARKINSON’S DISEASE PATIENTS WITH DIFFERENT TREATMENT PATTERNS: PROSPECT STUDY

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Background and Aims:: There is limited prospective real-world data describing the long-term changes in clinical outcomes and disease burden for individual advanced PD patients. The understanding of the treatment patterns and their differential impact over time is also limited. We describe the changing clinical outcomes and disease burden of advancing Parkinson’s disease in patients with motor fluctuations no longer controlled by current PD medications.

Methods:: PROSPECT is a 24-month, prospective, observational study of advanced PD patients (>30 years of age) no longer adequately controlled by their current therapy and have a minimum of 2.5 hours of “Off” time per day. Study assessments will be performed at baseline (ie, study enrollment) and 4 follow-up visits at months 6, 12, 18, and 24. Assessments will include the current treatment regimen, severity of disease (H&Y stage), changes in motor (“Off” and dyskinesia time) and non-motor symptoms (NMS scale and PD Sleep Scale-2), activities of daily living (UPDRS II), quality of life (PD Questionnaire-39 and EQ-5D), cognitive function (Mini-Mental State Evaluation), health care resource utilization, caregiver burden (Modified Caregiver Strain Index), treatment satisfaction and patient global impression of change in severity (PGIC-S). Comparative assessments between patients with different treatment patterns will occur at baseline to month 12 and month 24.

Results:: This study will enroll approximately 550 advanced PD patients from an estimated 90 multinational sites.

Conclusions:: This study will describe real-world long-term prospective insights on the natural progression of disease burden, clinical outcomes, and potential value of timely initiation of advanced therapies among patients with advanced PD.
A RETROSPECTIVE STUDY EVALUATING THE USE OF ANTI-PARKINSONIAN MEDICATIONS IN PATIENTS WITH ADVANCED PARKINSON’S DISEASE TREATED WITH LEVODOPA-CARBIDOPA INTESTINAL GEL AND DEEP BRAIN STIMULATION

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Background and Aims:: Patients using deep brain stimulation (DBS) with adjunctive oral therapy may require additional therapies like levodopa-carbidopa intestinal gel (LCIG), known as CLES in the United States. We examine use of oral/transdermal anti-parkinsonian medications in advanced Parkinson’s disease (APD) patients with history of or current treatment with DBS, receiving LCIG.

Methods:: PD-DUAL, a multicenter, US study included APD patients with history of DBS and ≥2 recorded visits before LCIG initiation and 2 visits (6 months) follow-up after LCIG initiation. Primary endpoint is mean decrease of oral levodopa-equivalent daily dosage (LEDD) during a 16-hour waking day after LCIG initiation from baseline to 6 months. Secondary endpoints include percentage of individuals with reductions from baseline in total oral levodopa daily dose after LCIG initiation, latency from LCIG initiation until introduction/tapering of each PD medication, and percentage of patients treated with DBS and LCIG for whom LCIG is a monotherapy.

Results:: As of 10 July 2020, 34 patient records were evaluable. The mean age is 67 years and 73% are male. Of 34 patients, 31 (91.2%) were taking levodopa-containing medications and 25 (73.5%) were taking non levodopa-containing anti-PD medications. For the primary endpoint, 20 patients had >75% reduction (10 patients with 100% reduction); 5 had >50% to ≤75% reduction; and 3 had 0 to ≤25% reduction. Two patients had no medication at baseline, and one had no reduction.

Conclusions:: Interim results demonstrated a median reduction of oral/transdermal LEDD (92%) 6 months post LCIG initiation in APD patients with a history of or current treatment with DBS.
NON-MOTOR SYMPTOMS AND THEIR IMPACT IN QUALITY OF LIFE IN MORROCAN PATIENTS WITH PARKINSON DISEASE: PROSPECTIVE STUDY:

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Background and Aims:: INTRODUCTION: Patients with Parkinson disease (PD) are more impaired by Non-motor symptoms (NMS) than motor symptoms, especially in advanced stages. Unfortunately, in most cases, it is underdiagnosed and undertreated. The aim of this study is to evaluate the frequency of NMS and their impact on the quality of life in patients with PD.

Methods:: This is a prospective observational study conducted in the neurology department of Mohammed VI university hospital, on NMS in Moroccan patients with PD, using the non-motor symptoms questionnaire (NMSQ) and the Parkinson's disease quality of life questionnaire Summary Index score (PDQ-39IS).

Results:: We report 115 patients (Males 61.5%) diagnosed over a period of 18 months. The mean age of onset was 53.71 (ranged from 23 to 76 years). Pain (60.3%), constipation (59%), urinary urgency (52.6%), sleep disturbances (57.7), and depression (47.4%), were the most frequent NMS in our cohort, while hallucinations (29.5%), diplopia (12.8%) and memory impairment (30.8%) were less frequent. Depressed mood, anxiety and sleep problems were more common in females, while urinary disorders, constipation, sexual dysfunction were more common in males. NMS are positively correlated to the H&Y stage and to duration of the disease. Our results showed that the impact affected mainly the emotional well-being (47, 81%). Mobility was affected in second place (44.13%), followed by daily activities (42, 9%).

Conclusions:: Conclusio: NMS can be very disabling and should be treated in the different stages of the disease. They can also be responsible of a decreasing on the patient's quality of life.
DISEASE SEVERITY IN THE DUOGLOBE PATIENT POPULATION BASED ON MANAGE-PD SECTION 2 DOMAINS: INTERIM SUBGROUP ANALYSIS

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Background and Aims:: DUOGLOBE is an ongoing global, observational study assessing long-term effectiveness of levodopa-carbidopa intestinal gel (LCIG) in advanced Parkinson’s disease (APD) patients (NCT02611713). This post-hoc analysis assessed disease burden among subgroups of DUOGLOBE patients based on the frequency/severity of symptoms in the domains of Section 2 of MANAGE-PD, a clinician-reported screening tool to identify APD patients uncontrolled on oral/transdermal medications.

Methods:: MANAGE-PD Section 2 domains were applied at baseline to DUOGLOBE patients. Patients were grouped by 1+, 3+, or 6 affected domains. Domains include “Off” time, troublesome dyskinesias, freezing of gait during “Off” time, falls, ADL impairment, and hallucination/psychosis. Efficacy and safety outcomes (Table 1) were evaluated at baseline and for mean change from baseline to Month 24 (M24).

Results:: Of 176 patients with available Section 2 responses, 94.3%, 42.6%, and 1.7% had a high enough frequency/severity in 1+, 3+ or 6 Section 2 domains, respectively. For patients with 1+ or 3+ affected domains, all efficacy outcomes improved from baseline to M24 except UPDRS II. Patients with more domains affected demonstrated greater numerical improvement. AE incidences were similar across groups.

Conclusions:: A high percentage of patients demonstrated frequent/severe enough symptoms in at least 1 MANAGE-PD Section 2 domain at baseline prior to LCIG, indicating insufficient symptom control. At M24 all groups showed improvements in key outcome measures. The subgroups with 3+ and 6 domains have higher disease severity; however, only 1 affected domain of MANAGE-PD Section 2 is required to consider device-aided therapy. Safety data were consistent with the profiles from phase 3 trials.

Table 1. Mean Change from Baseline to Month 24 for Affected MANAGE-PD Section 2 Domains in DUOGLOBE Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>1+ Domains</th>
<th>3+ Domains</th>
<th>6 Domains</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Change from Baseline to 24 months mean ± SD</td>
<td>Change from Baseline to 24 months mean ± SD</td>
<td>Change from Baseline to 24 months mean ± SD</td>
</tr>
<tr>
<td>OFF time</td>
<td>100</td>
<td>-3.8 ± 3.23</td>
<td>43</td>
</tr>
<tr>
<td>U DysRS</td>
<td>85</td>
<td>-9.3 ± 21.97</td>
<td>37</td>
</tr>
<tr>
<td>NMSS</td>
<td>106</td>
<td>-24.4 ± 43.7</td>
<td>43</td>
</tr>
<tr>
<td>UPDRS II</td>
<td>102</td>
<td>-6.3 ± 22.83</td>
<td>42</td>
</tr>
<tr>
<td>PDQ-8</td>
<td>70</td>
<td>-2.7 ± 7.61</td>
<td>33</td>
</tr>
</tbody>
</table>

Patients were grouped based number of affected domains of MANAGE-PD section 2. APD = advanced Parkinson’s Disease; LCIG = levodopa carbidopa intestinal gel; SD = standard deviation; U DysRS = Unified Dyskinesia Rating Scale; NMSS = Non-motor Symptoms Scale; UPDRS II = Unified Parkinson’s Disease Rating Scale; PDQ-8 = Parkinson’s Disease Questionnaire-8; MCSI = Modified Caregiver Strain Index.
FIRST EXPERIENCE IN THE UNITED STATES WITH TRUE REMOTE PROGRAMMING IN DEEP BRAIN STIMULATION THERAPY FOR MOVEMENT DISORDERS

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Background and Aims:: DBS in Parkinson’s disease and Essential tremor requires multiple in-person programming sessions burdening patients and caregivers. The recent FDA approved NeuroSphere™ Virtual Clinic enables clinicians for the first time to remotely connect into patient IPGs to perform system checks and actively adjust stimulation parameters. This is the first report describing clinical workflow and experience with the platform.

Methods:: 15 patients provided signed written consent to Abbott or verbal consent to the Clinician to be enrolled. The enrolled Abbott Infinity™ IPGs were securely mapped to authorized Clinicians. Software on programming devices was upgraded without requiring any hardware or firmware changes. Patients initiated remote sessions and Clinicians securely connected to the IPGs using unique logins and multi-factor authentication. Stimulation changes were synchronized with integrated video and a failsafe mechanism ensured continuity of therapy in case of network failure.

Results:: Of 15 DBS patients, 13 have undergone remote programming. The average time to establish connection has been less than 1 minute. There has been no perceptible difference in running system checks and of the order of 1 second for stimulation changes. Both English and Spanish speaking patients reported no difficulties using the platform. In one patient dysarthria was resolved and in another patient battery replacement was recommended remotely.

Conclusions:: Remote programming with this new platform is both clinically viable and meaningful. We expect to collect more objective metrics including impact on QoL, access, change in perceived quality of care with the adoption of this technology by both patients and neurologists.
MENTAL FLEXIBILITY IN PARKINSON’S DISEASE WITH CENTRAL FATIGUE: DATA FROM THE FRONTAL ASSESSMENT BATTERY

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\textbf{Background and Aims::} Central fatigue is defined as a reduced energy level or an increased perception of effort, often associated to a failure in initiating and maintaining tasks that require self-motivation. It is common in Parkinson's disease population and it has been hypothesized to be related to a dysfunction in the striato-thalamo-prefrontal loop. The aim of the present study was to explore the association between fatigue and executive functions as index of integrity of the striato-thalamo-prefrontal loop.

\textbf{Methods::} Twenty-nine non-demented PD patients without fatigue - PDnF, 28 non-demented PD patients with fatigue - PDF and 26 age and sex-matched controls underwent an evaluation with the Frontal Assessment Battery (FAB), MMSE, PSQI, BDI, STAI Y1-2, PDQ-39. Differences between groups in FAB scores (total and subitems) were analyzed by means of Kruskal-Wallis test. Moreover, a correlation between fatigue and FAB was also analyzed.

\textbf{Results::} Overall parkinsonian population displayed worse performance than controls in frontal scores especially inhibitory control (p=0.008) and sensitivity to interference (p=0.014). PDF displayed significantly worse than PDnF in verbal fluency (p=0.05). Fatigue severity inversely correlated with executive performance (p<0.001).

\textbf{Conclusions::} Phonemic fluency tasks are thought to reflect the simultaneous engagement of several executive functions such as attention, working memory, retrieval, information processing. The association of central fatigue with a deficit in mental flexibility, could support the hypothesis that central fatigue is a reliable index of the impairment of higher executive functions needed in order to effectively assess costs and benefits related to adaptive decision-making behavior.
POST ANOXIC MYOCLONIC ENCEPHALOPATHY SYNDROME OR LANCE- ADAMS: CASE REPORT

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Background and Aims:: Introduction: Lance Adams syndrome (LAS) a post anoxic myoclonic encephalopathy, an infrequently described entity since 1963, currently less than 200 cases have been reported1, characterized by myoclonic limb-acting movements and cerebellar ataxia with generally preserved higher mental functions, which typically appears hours or days after a cerebral hypoxia event (prolonged hypotension, cardiorespiratory arrest) and certain structures of the brain stem, cerebellum and diencephalon are thought to be involved in myoclonus due to hypoxia1-5.

Methods:: Case report

Results:: Case report: 60-year-old male patient with a history of systemic arterial hypertension, chronic renal failure under renal replacement therapy, presented cardiorespiratory arrest due to dialysis emergency, with successful cardiopulmonary resuscitation, post-resuscitation management in the critical care unit; presenting 24 hours later, persistent myoclonic movements of facial action and upper extremities that increased with sensory stimuli. Brain tomography (CT) and brain magnetic resonance (MRI) showed punctate hyperintensities in T2 and FLAIR in the basal ganglia, hippocampus and cerebellar vermis (Figure 1). Management with clonazepam and valproic acid was started with good response. One month later she presented mild cerebellar ataxia, without myoclonic movements, with preserved higher mental functions.

Conclusions:: In SLA, action myoclonias can also be triggered by different stimuli (tactile, sonorous, emotional), predominantly involving the extremities, with preservation of higher mental functions being a fundamentally clinical diagnosis; neuroimaging is usually normal and sometimes functional PET or SPECT studies are necessary, demonstrating increased glucose consumption in affected areas.1. Treatment is symptomatic, the first choice being clonazepam, valproic acid and levetiracetam with favorable clinical response. 1-5.
PREVALENCE OF VITAMIN B1 DEFICIENCY IN SUBJECTS WITH ADVANCED PARKINSON’S DISEASE SYMPTOMS

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Background and Aims:: Vitamin deficiencies impact neurological conditions and may present as progression of Parkinson’s Disease (PD). We have previously shown 6.1% of a cohort of subjects with PD were deficient in Vitamin B1 and that dietary intake of vitamin B1 was significantly lower in those with deficiency (p = 0.02). Here, we aim to assess the prevalence of serum vitamin B1 deficiency in subjects with advanced PD symptoms.

Methods:: Prospective enrollment of subjects was conducted within a PD Comprehensive Clinic. The ordinal scores (0-4) for postural stability, gait and arising from chair from the Unified Parkinson’s Disease Rating Scale (UPDRS) motor score evaluation and serum vitamin B1 were collected as part of routine care. A Harvard Food Frequency questionnaire was administered to quantify dietary intake. Percent of subjects with Vitamin B1 deficiency were evaluated within each available ordinal score and a Pearson Chi-Square exact test was used to compare groups. A p-value <0.05 was considered statistically significant.

Results:: In our analysis of 169 subjects with PD, the percent of patients with Vitamin B1 deficiency was significantly higher in the most severe symptom category for gait (0=10.5%, 1=9.1%, 3=13.0%, 4=50%; p=0.08) and arising from chair (0=8.33%, 1=10.2%, 3=50%, 4=N/A; p=0.002). Percent of deficient patients was also higher in patients with worsening postural stability (0=8.6%, 1=5%, 2=35.6%, 3=16.7%; p=0.007).

Conclusions:: A high percentage of PD patients with severe motor symptoms have vitamin B1 deficiency. Further research on the relationship between vitamin deficiencies and motor outcomes in PD patients is warranted.
Background and Aims: Little is known about the neuropsychiatric dimension of Parkinson disease in Moroccan patients. The aim of this work is to investigate the neuropsychiatric profile of Parkinson disease and the impact of symptoms on quality of life in a Moroccan cohort in an academic hospital.

Methods: A structured questionnaire, the Neuropsychiatric Inventory (NPI) and the Parkinson disease questionnaire (PDQ-8) were administered to a cross-section of 32 patients diagnosed with idiopathic Parkinson disease in the movement disorder clinic of the Mohammed VI University Medical Center of Marrakesh, Morocco.

Results: A slight male predominance was observed (sex ratio: 1.1). Age, onset and duration of disease were 58.5±9.3, 51.4±9.4, and 7.2±4.2 years respectively. All patients were on L-dopa; 25% were on antidepressants. The presence of neuropsychiatric symptoms was noted in 90.6% of patients, with clinically significant symptoms in 84.3%. Depression (75%), anxiety (65.6%) and irritability (62.5%) were the most frequent symptoms. The mean total NPI score was 22.4±16.7, with females reporting higher means (t=2.8, p=0.008). For symptomatic patients, sleep problems were the most distressful (7.71±2.99). The mean number of symptoms was 4.2±1.8, with females reporting significantly higher numbers (t=2.56, p=0.016). The mean PDQ-8 score was 13.0±7.2. No difference was observed in terms of gender (t=0.27, p=0.79). A negative correlation was observed between age of onset and quality of life (r=-0.39, p=0.26).

Conclusions: Neuropsychiatric symptoms are frequent in our patients and do impact quality of life but remain under treated. As such, it is imperative to screen and treat them if present.
Background and Aims:: Quality of life (QoL) in Parkinson’s Disease (PD) worsens as bradykinesia, rigidity, rest tremor, gait disturbance, and cognitive changes progress over time. We searched for treatable conditions that masquerade as worsening PD. Vitamin deficiencies are common in PD patients, and many can cause neuropathies that worsen gait and cause falls. Deficiencies in B1 and B12 cause cognitive decline, and deficiencies in D increase the risk of fractures with falls. The goal of this research is to improve QoL in patients with PD by identifying and treating vitamin deficiencies.

Methods:: We collected 178 cases from our Comprehensive PD Clinic using prospective and retrospective methods. Statistical analyses were performed on serum vitamin levels (B1, B6, B12, and D), the United Parkinson’s Disease Rating Scale (UPDRS) Part III Motor Exam and the Harvard Food Preference Questionnaire.

Results:: 40% of patients had at least one vitamin deficiency. Deficiencies of vitamins B1, B6, B12, and D were found in 6%, 26%, 6%, and 30% respectively. Hallucinations disappeared within 3 days of oral replacement of low vitamin B1 in one patient. Many other patients improved or stabilized after vitamin replacement, especially if treated early.

Conclusions:: Vitamin deficiencies are “the Great Imitator” of PD progression and are correctable. A high index of suspicion, early detection, and aggressive correction of vitamin deficiencies can prolong and improve the QoL of PD patients. Future data analyses will look at changes in the UPDRS correlating with serum vitamin levels and how food preferences affect vitamin deficiency risk.
NEURORADIOLOGICAL FINDINGS IN HEMICHOREIC DISORDER AND GLYCEMIC DECOMPENSATION: CASE REPORT.

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Background and Aims:: Chorea and ballismus are involuntary movement disorders. Conditions such as cerebrovascular insufficiency, neurodegenerative, neoplastic, immunologic, infectious, and metabolic diseases are secondary causes of the disorder, with nonketotic hyperglycemia being the most common metabolic cause. Several reports describe on brain magnetic resonance imaging (MRI) unilateral hyperintense lesions of the putamen, caudate in T1; the etiology and pathogenesis is unclear, frequent in elderly women, strict glycemic control and neuroleptics leads to good prognosis in most patients. 1-5

Methods:: Caso report

Results:: Clinical Case

66-year-old woman with insulin-dependent type 2 diabetes mellitus and hypertension of 5 years of evolution, with unsatisfactory glycemic control in the last 2 years, consults for 2 days of evolution consisting of choreiform movements of the right body, laboratories show glycemia 348 mmol /L, HbA1c in 11.1%, plasma osmolarity 318 mOsm /L and negative ketonuria; compatible with non-ketotic glycemic decompensation, paraneoplastic syndromes were ruled out. Brain MRI showed occipital subacute lacunar infarcts and right semioval center, left peratral, microangiopathic leukoencephalopathy, left putamen hyperintensity in T1, T2 and FLAIR, diffusion pseudonormalization, with discrete enhancement with gadolinium (figure 1), spectroscopy with normal levels of metabolites without lactate peak.
Management with haloperidol and clonazepam, chorea started to resolve after 10 days of successful glycemic control.

**Conclusions:** The hemichorea observed in association with hyperglycemia, hyperintensity on T1-weighted MRI is universally recognized, the pathophysiologic mechanism remains unknown and these findings indicate that it is not simply due to cerebral infarction, but involves a vasculopathy exclusively restricted to the putamen and/or striatum in diabetic patients. 6-10
ESSENTIAL TREMOR AND COGNITIVE FUNCTIONING: A CLINICAL AND IMAGING STUDY

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Background and Aims:: The purpose of this case-control study was to characterize the neuropsychological profiles of patients with ET and to delineate its neuroanatomical counterpart.
Methods:: We collected neuropsychological, and MRI data from 49 non-demented ET and 50 age-, sex-, and education matched healthy controls. We performed (i)direct comparison between groups; (ii)machine learning analysis with feature selection to obtain the best discriminant tests between groups. The tests showing differences and/or the best discriminating ability were inserted in a whole-brain voxel-based-morphometry (VBM) correlation model in MRI to evaluate the correlation between cognitive performances and the degree of brain atrophy in the ET group without a priori hypothesis.
Results:: ET patients performed worse than HC in tests evaluating cognitive control, verbal and working memory (FAB p:0.05, MCST-CA p:0.029, RAVLT-DR p:0.03, Digit-SpanB p:0.03). The same tests and those for language evaluation had the greatest discriminating ability (RAVLT-DR, FAB, COWAT, RAVLT-IR). Regardless of the test explored, the MRI analysis revealed a strong (p<0.05 FWE, whole brain) correlation between tests (FAB, RAVLT-IR, RAVLT-DR, COWAT) and widespread areas including cerebellum, thalamus, inferior and middle frontal cortices, cingulate cortices, hippocampus, parahippocampal gyri, temporal cortex.
Conclusions: Our results suggest that ET-related cognitive impairment involves attention/executive function, memory, and language. Heterogeneity in the cognitive presentation goes along with broad involvement of many cerebral areas that include cerebello-thalamo-cortical loop and spread outside this network (hippocampus, parahippocampal gyri, temporal and cingulate cortices). Therefore, ET patients may develop disease-related changes beyond the cerebellar network, leading to broad cognitive damage.

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BETA-ADRENOCEPTOR ANTAGONISTS AND RISK OF PARKINSON’S DISEASE: META-ANALYSIS OF PHARMACOEPIDEMIOLOGICAL STUDIES

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Background and Aims:: Parkinson’s disease (PD) is exhibited by intracellular accumulation of Lewy Bodies (α-synuclein) encoded by α-synuclein gene. A possible relationship between β-adrenergics and α-synuclein synthesis has been shown. Pharmacoepidemiological (PE) studies evaluating β-antagonist use and risk of PD have reported conflicting findings. We performed a meta-analysis of PE studies evaluating the association of β-antagonist use and risk of PD.

Methods:: PubMed, Embase were searched from inception to Oct-2020. Two reviewers screened records in duplicate; PE studies reporting relative risk (RR) of PD in β-antagonist-users, compared to non-users, were included. Newcastle-Ottawa scales (NOS) was used to assess study quality. We employed generic inverse variance method using RevMan(5.3.5) to estimate pooled adjusted RR (aRR) using random-effects model. Sub-groups were analyzed based on study design and type of β-antagonist.

Results:: Of 1054 records, eight studies (2:cohort;6:case-control) with 6,267,037 participants (74,189 PD cases), were included. Significant heterogeneity (I\textsuperscript{2}>92\%) was observed; majority (n=7) of the studies were of moderate/high quality. In the overall pooled analysis (n=7) including any β-antagonist-users, compared with non-users, the aRR for PD was 1.27 (95\%CI:1.02,1.57;P= 0.03). The risk of PD, in β-antagonist-users, was significant for cohort studies (n=2) (aRR:1.78;95\%CI:1.24,2.57;P=0.002), and non-significant (aRR:1.08;95\%CI:0.92,1.27;P=0.34) for the case-control studies (n=5). By β-antagonist type, risk of PD was significantly higher only for the propranolol (aRR:1.91;95\%CI:1.20,3.06;P=0.007) and not for metoprolol (aRR:1.05;95\%CI:0.88,1.24;P=0.61), carvedilol (aRR:0.87;95\%CI:0.79,0.96;P=0.006), bisoprolol (aRR:0.93;95\%CI:0.60,1.43;P=0.73), sotalol (aRR:1.03;95\%CI:0.69,1.52;P=0.90), and atenolol (aRR:0.97;95\%CI:0.92,1.02;P=0.28) users.

Conclusions:: An increased risk of PD was observed in β-antagonist users that was driven mainly by propranolol use and not the other β-antagonists’ use, possibly indicating a protopathic bias.
Background and Aims:: Considering the evidences of neuronal protective effects of curcumin in previous in vitro, experimental animal and clinical studies, this double-blind, randomized, placebo-controlled, and parallel-group trial would explore the possible nanomicelle curcumin (SinaCurcumin®. Nano-Micellar Soft gel)-mediated impact on sleep, fatigue, and quality of life (QoL) in patients with Parkinson's disease (PD).

Methods:: Fifty PD patients were recruited and randomly divided into experimental (25) and control groups (25). Measurement tools were as follows: Hoehn & Yahr scale for stage of disease progression, sleep quality based on the Pittsburgh Sleep Quality Index (PSQI), fatigue based on Fatigue Severity Scale (FSS), and QoL based on the Parkinson's Disease Questionnaire–39 (PDQ-39) at the beginning and the end of the study. The groups were treated for three months by 80 mg of Nano-Micellar Soft gel twice a day.

Results:: Nanomicelle curcumin significantly increased sleep quality and QoL compared with placebo (P-values= 0.0001 and 0.0002, respectively) in PD patients. This significant difference was not influenced by the variables of the duration of the disease, stage of disease progression, and the dose of levodopa. This supplement did not have a significant effect on the fatigue severity of patients compared to placebo.

Conclusions:: Based on the results of this study, it is recommended that the nanomicelle curcumin can be used to improve sleep quality and QoL in PD patients.
COLONIC TRANSIT TIME IN PROGRESSIVE SUPRANUCLEAR PALSY AND PARKINSON’S DISEASE

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Background and Aims:: Gastrointestinal (GI) function in progressive supranuclear palsy (PSP) has not been reported, in contrast with extensive studies of GI function in Parkinson’s disease (PD). We aimed to investigate GI function in PSP and PD.

Methods:: A GI questionnaire for constipation and an objective colonic transit time (CTT) test were performed in 8 patients with PSP (6 men and 2 women; mean age, 74.6 years, mean duration of disease, 2.9 years), 36 patients with PD (19 men and 17 women; mean age, 75.6 years, mean duration of disease, 2.6 years) and 8 age-matched normal control subjects (4 men and 4 women; mean age, 73.6 years).

Results:: A GI questionnaire showed constipation in 2 (25%) PSP; 23 (64%) PD; and none (0%) control, without statistical significance. A CTT test showed total CTT of 63.2±33.9 hours in PSP; 69.6±42.8 hours in PD; and 45.2±40.3 hours in control, without statistical significance. In contrast, right CTT in PSP (p<0.05) and PD (p<0.01) was significantly prolonged from that in control.

Conclusions:: Subjective constipation is uncommon, but prolonged CTT is observed in PSP. This GI feature needs appropriate management and care, which might reflect PSP’s brainstem/sacral spinal cord pathology.
COMPREHENSIVE FUNCTIONAL EVALUATION OF THE SPECTRUM OF PROGRESSIVE NUCLEAR PALSY WITH 18F-FDG PET/CT AND 99MTC TRODAT-1 SPECT

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Background and Aims:: To elucidate the patterns of characteristic hypometabolism on 18F-FDG PET/CT in various subtypes of PSP and correlation with the core clinical features.

Methods:: A retrospective analysis of 124 patients of clinically suspected PSP was done. All the subjects were clinically analyzed and rated using the Progressive supra nuclear palsy rating scale proposed by the Movement Disorder Society by the Neurologist and were further clinically segregated into five subtypes-PSP with Richardson’s syndrome, PSP with predominant parkinsonism, PSP with speech/language presentation, PSP with frontal presentation and PSP with predominant ocular presentation. All the subjects underwent 99mTc TRODAT-1 SPECT study and 18F-FDG PET/CT scan on two separate days. The scans were analyzed qualitatively (visually) and semi-quantitatively and the FDG uptake patterns were recorded and areas of hypometabolism that were two standard deviations from the mean were considered as abnormal.

Results:: 99mTc TRODAT-1 scan was abnormal in all the subjects, establishing degenerative Parkinsonism. The subjects of PSP with Richardson’s syndrome showed diffuse hypometabolism involving anterior cingulate and orbital frontal cortices with diffuse hypometabolism involving basal ganglia, thalami, mid brain and sensori-motor cortices. In subjects with PSP with speech/language and frontal presentation variable additional involvement of the anterior and medial frontal association, insular and anterior temporal cortices was seen.

Conclusions:: Dopamine transporter imaging agent 99mTc TRODAT-1 SPECT helps in confirmation of degenerative Parkinsonian disorders. Characteristic patterns of hypometabolism may help in differentiation of the subtypes of PSP in the presence of clinically overlapping symptoms.
Background and Aims:: Most patients diagnosed with PD show gastrointestinal symptoms as one of the earliest features. For example, PD patients often complain of gastrointestinal distress such as constipation and nausea. It is important to note that about 60% of PD patients suffer from constipation, which can begin 20 years before diagnosis and is one of the prodromal syndromes.

Methods:: This is an overview abstract including analysis of researches regarding gut microbiota and Parkinson's disease.

Results:: The human gut microbiome has been shown to complement the host with basic functions and affect the host's central nervous system via the gut-brain axis through modulation of neural pathways and GABAergic pathways and serotonergic signaling systems. The human gut microbiome subsequently divided into three enterotypes: Ruminococcus, Bacteroides and Prevotella. Next generation sequencing protocols are widely used to both identify and characterize these communities. The gastrointestinal microbiota has essential functions to maintain metabolic homeostasis such as direct inhibition of overgrowth of pathogenic microorganisms, development of intestinal defenses, vitamin biosynthesis, energy modulation, and immunological and xenobiotic effects.

Conclusions:: Unfortunately, the relationship between the microflora of the gastrointestinal tract and the brain is not well understood. There are relatively few studies that highlight the relationship between intestinal flora and PD; It can be concluded that the broader significance of the human microbiome is complex and requires further research to improve the current understanding of the mechanisms underlying Parkinson's disease.
CONNECTION BETWEEN OLFACTORY DYSFUNCTION AND SEVERITY OF TREMOR

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Background and Aims:: Neurological disorders it's a problem for a number of people worldwide. Parkinson's disease (PD) and essential tremor (ET) are among them. Tremor is the common symptom both for PD (rest tremor) and ET (postural-kinetic tremor). Olfactory dysfunction is stipulated to be the first manifest of PD preceding the movement disorders. It happens due to the neurodegenerative process starting in olfactory bulbs. Currently available data on the olfactory function in ET are insufficient and some of them are contradictory. Hence, our aim was to obtain tremor data of PD and ET patients and the data of their olfactory function to verify our scientific hypothesis on the inverse relation between tremor manifestation and olfactory function decay: milder tremor is accompanied with worse smell perception, and vice versa.

Methods::

- Image of test tubes with different colored caps, likely used for medical or scientific purposes, placed on a table.
We had three groups of patients: PD, ET and healthy people. An examination procedure of olfactory function was based on Sniffin’ sticks test. For tremor testing we used wireless device to monitor electrophysiological signals. We used an elastic map technique to cluster and analyze all data.

Results:
Combination of tremor data and smell perception provides clear and apparent distinction of PD patients from ET ones. Proven inverse relation between tremor level and olfactory function decay is the most sounding result of our work. Indeed, ET patients showed better olfactory function results accompanied by stronger tremor, as compared to PD patients.

**Conclusions:** The presented results could be implemented for early differential diagnostics of PD, ET, as well as for the improvement of individual therapy for such patients.
SUSTAINED RELEASE TRIPLE DRUG LOADED COLLOIDOSOMES FOR MANAGEMENT OF PARKINSON’S DISEASE

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Background and Aims:: Parkinson’s disease (PD) is well-known as a progressive and degenerative disease of nervous system. The degeneration of dopaminergic neurons in substantia nigra, and reduction in amount of neurotransmitter dopamine available in striatum relate symptoms of this disease. It is hypothesized that a drug delivery system that provides controlled and sustained release of PD drugs would afford better management of PD. Hollow microcapsules composed of PMMA (polymethyl methacrylate) and poly(caprolactone)(PCL) are prepared through a modified double-emulsion technique. They are loaded with three PD drugs, i.e., levodopa(LD), carbidopa(CD), and entacapone(ENT), at a ratio of 4:1:8.

Methods:: Microcapsules were prepared through a double emulsion(W1/O/W2) solvent evaporation method with modifications to produce hollow microspheres. Microcapsules were then spray coated along with ENT. Shape and surface morphology were studied using SEM & TEM. Average particle size and polydispersity index were determined by optical microscopy, drug entrapment, CLSM, Buoyancy tests and in-vitro drug release was studied.

Results:: LD and CD are localized in both hollow cavity and PMMA/PCL shell, while ENT is localized in PMMA/PCL shell. Release kinetics of hydrophobic ENT is observed to be relatively slow as compared to other hydrophilic drugs. It is further hypothesized that encapsulating ENT into PCL as a surface coating onto these microcapsules can aid in accelerating its release. Now, these spray-coated hollow microcapsules exhibit similar release kinetics, according to Higuchi’s rate, for all three drugs.

Conclusions:: Results suggest that multiple drug encapsulation of LD,CD, and ENT in gastric floating microcapsules could be further developed for in-vivo evaluation for management of PD.
Background and Aims:: Patients with essential tremor and adductor-type spasmodic dysphonia may manifest a prominent voice tremor. The diagnosis of voice tremor is currently based on perceptual and qualitative analysis. We have recently demonstrated in two independent studies that advanced voice analysis with machine learning objectively discriminates normal voices from those recorded from patients with essential tremor and dysphonia. The aim of this study is to achieve a direct and objective discrimination between voice samples recorded from patients with essential tremor and dysphonia both manifesting voice tremor.

Methods:: We investigated 33 patients with adductor-type spasmodic dysphonia (7 males, 65.6±11.7y), 36 patients with essential tremor and voice tremor (9 males, 72.4±8.6y), and 74 age-matched controls (20 males, 71.0±12.4y). We recorded voice samples during sustained vowel emission using a high-definition audio recorder. The classification of voice samples was achieved by means of a dedicated machine learning algorithm.

Results:: Receiver Operating Characteristic curves showed that machine learning objectively discriminated between controls and essential tremor (Accuracy: 96.1%; AUC: 0.95), controls and dysphonia (Accuracy: 97.5%; AUC: 0.97) and finally essential tremor and dysphonia (Accuracy: 97.5%; AUC: 0.97).

Conclusions:: Advanced voice analysis using machine learning objectively recognize voice tremor in patients with essential tremor and dysphonia discriminating the two forms of voice tremor with high accuracy. Our findings suggest that voice tremor differs in patients with essential tremor and spasmodic dysphonia. This finding points to different pathophysiological mechanisms underlying voice tremor in the two conditions.
BRAIN ACTIVITY IN THE IDIOPATHIC PARKINSON'S DISEASE

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Background and Aims:: We used a high-density electroencephalography (HD EEG) to investigate changes in bioelectric potentials and potentially changes in connectivity between STN and IFC in patients with Parkinson's disease after deep brain stimulation (DBS).

Methods:: A prospective observational descriptive study in patients with DBS therapeutic intervention was chosen as a research design realised in the period between 2017 and 2020. A connectivity between subthalamic nucleus and inferior frontal cortex was observed during double-task cognitive non-motor task in patients with DBS stimulator turned off and on. The main examination method used was HD EEG with 256 channels.

Results:: A total of 32 patients were contacted during standard outpatient check-ups, eight (25 %) patients agreed to participate in the study. The average age of the patients was 66.7 years (range 57 – 76 years). At the end of the study decrement of the connectivity between IFC and STN for target stimuli after the DBS was switched ON in patients on dopaminergic medication was observed. This decrease may partly explain the negative effect on cognitive functions of the DBS STN therapeutic method in previously published studies.

Conclusions:: The decrease of connectivity between IFC and STN was identified. There was no difference in laterality of connectivity decrease. We therefore assumed that DBS stimulation during the medication ON state disrupted functional connectivity between IFC and STN. The study results forms new hypotheses in the field of brain connectivity in IPD patients. Further study is needed to confirm our hypotheses.
CLINICAL CHARACTERISTICS OF PARKINSON’S DISEASE IN SUDANESE PATIENTS ATTENDING DAOUD CHARITY CLINIC IN 2020-2021.

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Background and Aims:: Introduction: Parkinson’s disease (PD) is the second most common neurodegenerative disorder, after Alzheimer’s disease. Parkinson’s disease main four clinical features include muscle rigidity, tremors, and bradykinesia and gait. Also there is secondary features like depression, emotional change, dementia, constipation, postural hypotension, changes in speech, skin problem, and dysphagia. Objectives: To identify the clinical features of Parkinson disease in Sudanese Parkinson’s patients.

Methods:: A descriptive cross sectional clinic based study during the period of January 2020 to January 2021. Data was collected using unified Parkinson disease rating scale via trained doctors on interview based clinic setting with full medical history and physical examination.

Results:: This study includes 35 patients with Parkinson disease 25 (71, 4%) were male and 10 (28, 6%) were female. The most common age of the patients ranges from 61 to 70 years (34, 5%). Bradykinesia was found to be the most common symptoms (85, 7%) more than rigidity (82, 9%), tremor (74, 3%) and postural gait instability (71, 4%).

Conclusions:: This study has identified the most common clinical features of Parkinson’s disease. The present study confirms previous findings, notwithstanding the relatively limited sample, this work offers valuable insights into the clinical presentation of Parkinson disease in Sudanese
ASSESSMENT OF FRONTAL LOBE FUNCTIONS IN PARKINSONISM SYNDROMES

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Background and Aims:: Frontal lobe dysfunction is a predominant feature of progressive supranuclear palsy however it can be present in other parkinsonism syndromes also. The frontal assessment battery (FAB) is a brief tool developed to assess frontal lobe functioning at bedside Objective: To assess the frontal lobe functions in patients with Parkinsonism syndromes

Methods:: 110 study subjects who fulfilled the inclusion and exclusion criteria were included in the study over a period of 10 months They were clinically evaluated for frontal lobe dysfunction using the FAB battery during the ON and OFF period. Collected data was coded and entered in Microsoft Excel and data was analyzed using SPSS software version 20

Results:: Results: . The mean MMSE score of the population during the ON and OFF period was 25.09 +/-1.8 and 25.05+/-0.8. In terms of FAB scores, the mean value of the study population during ON and OFF periods were 11.18+/- 2.9 and 10.95+/- 2.8 respectively. The mean difference between the FAB scores during the ON and OFF period was 0.24 which was statistically significant (p=0.018). There was significant difference between the frontal lobe dysfunction during the ON and OFF period (p <0.05).

Conclusions:: Conclusion: Frontal lobe dysfunction during the ON period was found in 54.5% of the total study population In the OFF period 60% of the total study population had frontal lobe dysfunction. The maximum dysfunction was found in PSP and minimum in CBD during both ON and OFF period.
ASSESSMENT OF NON MOTOR SYMPTOMS IN PARKINSONISM SYNDROMES

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Background and Aims: BACKGROUND: James Parkinson described Parkinson’s disease in 1817. He described the motor and non motor findings in Parkinson’s disease. Despite this emphasis on motor symptomatology, several studies have shown that the non-motor symptoms of Parkinson’s disease, such as depression, psychosis, falls, and sleep disturbance, have greater significance when assessed by quality-of-life measures, institutionalization rates, or health economics. OBJECTIVE: To study the prevalence and duration of non motor symptoms in patients with parkinsonism syndromes

Methods: MATERIALS AND METHODS: 110 study subjects who fulfilled the inclusion and exclusion criteria were included in the study. Non Motor Symptom history was obtained using a questionnaire. Collected data was coded and entered in Microsoft Excel and data was analyzed using SPSS software version 20.

Results: RESULTS and DISCUSSION: - The prevalence of non motor symptoms was 97.3% of the total study population. The mean duration of Non Motor symptoms in the study population was 3.28 +/- 2.74 yrs. In IPD pts the mean duration was 4 +/- 3.5 yrs, in PSP was 2.13 +/- 1.88 yrs, in MSA was 2.16 +/- 1.83 yrs, and in CBD was 3 +/- 2.16 yrs and in vascular Parkinsonism it was 2.97 +/- 2.39 yrs. 23.6 % of the study population had postural hypotension.

Conclusions: CONCLUSION: - The most common symptom in the total population was gastroenterological symptoms and fatigue (60%) and the least common symptom was skin problems (0.9%). Skin and respiratory problems were least encountered non-motor symptoms.
METABOLIC CONCENTRATIONS, T2 VALUES PATIENTS WITH PARKINSON'S DISEASE (PD) AS BIOMARKERS OF THE LEVEL OF COGNITIVE IMPAIRMENT (CI)

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Background and Aims:: To evaluate the level of CI in PD-patients we study the relaxation times and content of the main cerebral metabolites in the frontal lobe (FL) and in putamen (P).

Methods:: 18 PD-patients of 1st group (DPDG) with dementia (MMSE<25), 16 - 2nd (CIPDG) with mild CI (30≥MMSE≥25), 16-3rd (NPDG) with (MMSE≥30), 15 controls of 4th (CG) are studied by 1.5T SIGNA HDxt(GE). 1H spectra are obtained in FL and in P.

Results:: In FL the shortening of the T2M for all of the patients are found. T2M in FL: 67.1, 40.5, 98.6ms (DPDG); 145.2, 59.3, 207.5ms (CIPDG); 210.1, 185.3, 263.4ms(NPDG); 204.2, 198.0, 331.2ms(CG). These allow us to distinguish subjects of CG from PD-patients, but they are not specific for evaluation of the level of CI. T2M in P: 63.3, 56.5, 101.8ms(DPDG); 58.2, 49.0, 90.2ms(CIPDG); 134.1, 152.3, 233.1ms(NPDG); 215.0, 114.0, 320.1ms(CG). In P NAA/Cr ratios in DPDG and CIPDG are significantly lower than in the NPDG, Cho/Cr ratios higher than in NPDG. Content of NAA in P:(6.81+-1.8), (7.62+-1.4), (7.82+-1.3) in DPDG, CIPDG, and NPDG, and NAA/Cr decrease with the grade of CI. Concentrations of mIns in FL: (4.23+-0.79), (3.69+-0.62), (3.43+-0.83) in DPDG, CIPDG, and NPDG, and mIns/Cr increase with the grade of CI. Concentrations of Glx in FL is more pronounced, than other metabolites:(8.1+-1.9), (9.32+-1.6), (10.6+-1.8) in DPDG, CIPDG, NPDG, and Glx/Cr decrease with the grade of CI. Concentration of Glx in the BG: (6.34+-1.4), (7.93+-0.9), (9.46+-1.2) in DPDG, CIPDG, NPDG. We have found the progressive decreasing Glx-content in the FL and in P for the patient of NPDG, CIPDG, DPDG, that is associated with poorer cognitive function.

Conclusions:: T2M, concentration may be of CI.
Background and Aims:: Stiff Person Syndrome (SPS) is a rare autoimmune neurological disorder, characterized by axial and limb muscular stiffness and spasms, due to a loss of physiological GABAergic CNS inhibition. In 60%-80% of patients with classic SPS phenotype antibodies against glutamic acid decarboxylase (GAD) enzyme can be detected.

Methods:: All patients with a clinical diagnosis of SPS and GAD antibodies, evaluated at Ospedale Maggiore Policlinico, Milan, Italy, between 2013 and 2021, were retrospectively included. The presence of GAD antibodies was screened by quantitative assessment (either Chemiluminescent immunoassay-CLIA or Radioimmunoessay-RIA), and subsequently confirmed by qualitative assessment (Western Blot and immunohistochemistry.)

Results:: 9 patients were included, all of female gender. The mean age at onset was 42.7 years (25-61). The most common symptoms at onset were unexplained falls and dorso-lumbar pain. Three patients suffered from poorly controlled autoimmune diabetes; positivity to anti-thyroglobulin, anti-thyreoperoxidase and anti-parietal gastric cells was also detected. One patient had history of partial epilepsy, and other 3 patients had subclinical epileptic activity on EEG. All patients had a good response to symptomatic treatment with either clonazepam or baclofen (in one case with intrathecal pump), but were also treated with immunotherapy, with either plasma-exchange or IVIG in inpatient setting, and subsequently with second-line agents (Rituximab, Azatioprine, Methotrexate). Two patients underwent thymectomy, with identification of thymic hyperplasia vera, although with no symptomatic relief.
Conclusions: GAD associated SPS is a protean syndrome, with diverse neurological manifestations combined with autoimmune disorders. A patient-tailored combination of symptomatic drugs and immunotherapies is needed to improve the patients' quality of life.
CLINICAL UTILITY OF DOPAMINE TRANSPORTER SCAN (DAT SCAN) IN CLINICALLY SUSPECTED PARKINSONISM: A TERTIARY CARE CENTER EXPERIENCE

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Background and Aims:: The most sensitive imaging techniques for an early diagnosis of parkinsonian syndromes are SPECT and PET, with DaT scan reported to be widely used with effective management of PD. Aims and objectives: The objective of this study is to assess the impact of 123I-ioflupane SPECT i.e. (DaT SCAN) on the diagnosis and management along with assessing its safety profile in Kuwait

Methods:: We analyzed retrospectively the DaT scan referral forms, history data and official reports from the nuclear medicine department of Ibn Sina hospital in Kuwait between January 2018 to January 2020. All referring physicians were contacted in order to assess the impact of the scan on the diagnosis and management of those patients.

Results:: Table 1: Clinical utility

<table>
<thead>
<tr>
<th>Provisional clinical diagnosis</th>
<th>Number (percent to total number of Dat scans)</th>
<th>No change post Dat (percent to provisional diagnosis)</th>
<th>Change in diagnosis ± treatment (percent to provisional diagnosis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential tremors</td>
<td>14(20.6%)</td>
<td>11(78.6%)</td>
<td>3(21.4%)</td>
</tr>
<tr>
<td>Drug induced parkinsonism</td>
<td>11(16.2%)</td>
<td>8(72.7%)</td>
<td>3(27.3%)</td>
</tr>
<tr>
<td>Degenerative parkinsonism</td>
<td>34(50%)</td>
<td></td>
<td>11(32.35%)</td>
</tr>
<tr>
<td>DLB</td>
<td>3(4.4%)</td>
<td>1(33.3%)</td>
<td>2(66.7%)</td>
</tr>
<tr>
<td>Vascular parkinsonism</td>
<td>2(2.9%)</td>
<td>1(50%)</td>
<td>1(50%)</td>
</tr>
<tr>
<td>Psychogenic tremors</td>
<td>2(2.9%)</td>
<td>0(0%)</td>
<td>2(100%)</td>
</tr>
<tr>
<td>Orthostatic tremors</td>
<td>2(2.9%)</td>
<td>1(50%)</td>
<td>1(50%)</td>
</tr>
<tr>
<td>Total</td>
<td>68</td>
<td>45(66.2%)</td>
<td>23(33.8%)</td>
</tr>
</tbody>
</table>

Table 2: Results of DaT scan

<table>
<thead>
<tr>
<th>Result N=68</th>
<th>Positive (47%)</th>
<th>Negative (48.5%)</th>
<th>Equivocal (4.5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>Grade 1</td>
<td>Grade 2</td>
<td>Grade 3</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2</td>
<td>28</td>
</tr>
</tbody>
</table>

Conclusions:: Normal binding of 123I-Ioflupane to presynaptic transporters rules out, with a high diagnostic accuracy, the presence of IPD or other parkinsonian syndromes with high safety standards.
DYSAUTONOMIA IN IDIOPATHIC PARKINSON’S DISEASE: RELATIONSHIPS WITH DISTRIBUTION OF MOTOR SYMPTOMS AT ONSET

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Background and Aims:: Dysautonomia is a common and disabling non-motor symptom (NMS) of Parkinson’s disease (PD), most frequently occurring in advanced patients. Some NMSs of PD, including cognitive and sleep disturbances, showed associations with lateralization of motor symptoms at onset. In this retrospective study, we investigated the relationships between motor features at onset and dysautonomia.

Methods:: Medical records from 308 PD patients referring to our Movement Disorder Service between 2015 and 2020 were screened for the presence of dysautonomia. This was defined as a score ≥2 in at least one of the “cardiovascular”, “genitourinary” or “gastrointestinal” items of the PD-Non Motor Symptoms Scale (NMSS). Lateralization of symptom onset was defined by at least 2-point left-right difference at the MDS-UPDRS-III score. Patients were divided according to the distribution of motor symptoms at onset as left side (LO, n=145), right side (RO, n=129) or bilateral (BO, n=34).

Results:: There were no demographic, clinical and therapeutic differences among the three groups. BO patients displayed higher prevalence of cardiovascular, gastrointestinal and urinary symptoms compared to LO and RO (41% vs. 21-24%, 59% vs. 52-43%, 71% vs. 50-47%, respectively). Moreover, BO patients displayed a higher prevalence of co-existence of all three dysautonomic domains (14%, p=0.008). There were no significant differences between LO and RO patients.

Conclusions:: PD patients devoid of clear lateralization of motor symptoms at onset are more prone to develop dysautonomic symptoms. This may contribute to determining stronger disability.
DEEP BRAIN STIMULATION IN HUNTINGTON'S DISEASE.

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Background and Aims:: Huntington’s disease (HD) is an inherited neurodegenerative disorder clinically characterized by involuntary movements, cognitive decline, and behavioral changes. The complex constellation of clinical symptoms still makes the therapeutic management challenging. We evaluated the effects of deep brain stimulation (DBS) on patients affected by HD, providing a critical outlook on the achieved results and the possible developments.

Methods:: Articles describing the effect of DBS in patients affected by HD were selected from Medline and PubMed by the association of text words with MeSH terms as follows: “Deep brain stimulation”, “DBS”, and “HD”, “Huntington’s disease”, “Huntington”. Details on repeat expansion, age at operation, target of operation, duration of follow-up, stimulation parameters, adverse events, and outcome measures were collected.

Results:: Twenty eligible studies, assessing 42 patients with HD, were identified. The effect of GPI-DBS on Unified Huntington's Disease Rating Scale (UHDRS) total score revealed in 10 studies an improvement of total score from 5.4% to 34.5%, and in 4 studies an increase of motor score from 3.8% to 97.8%. Bilateral GPI-DBS was reported to be effective in reduction of Chorea subscore in all studies, with a mean percentage reduction of 21.4% to 73.6%.

Conclusions:: HD patients with predominant choreic symptoms may be the best candidates for surgery, but the role of other clinical features and of disease progression should be elucidated. For this reason, there is a need for more reliable criteria that may guide the selection of HD patients suitable for DBS. Accordingly, further studies which have functional outcomes as primary endpoint are needed.
A BRAINSTEM HYPERMETABOLISM IN A PATIENT WITH ESSENTIAL PALATAL TREMOR: A SIMULTANEOUS 18F-FDG-PET/3T-MRI STUDY

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Background and Aims:: Essential palatal tremor (EPT), previously referred as palatal myoclonus, is a rare movement disorder characterized by rhythmic and continuous jerks of soft palate [1]. While symptomatic palatal tremor (SPT) is typically caused by brainstem or cerebellar lesions [2], pathogenetic mechanism underlying EPT remains debated [1]. Here we reported a simultaneous brain fluorine-18-fluorodeoxyglucose-positron emission tomography (18F-FDG-PET)/3T- magnetic resonance imaging (MRI) study in a woman with EPT.

Methods:: A 54-year-old woman presented to our Neurological Department reporting as isolated manifestation a bilateral ear clicking started at the age of 20 years. She referred the “click” was perceived constantly, except during sleep, and worsened by stressful situations. The neurological examination revealed palatal movements lifting posterior soft palate, including the uvula, synchronous to an audible outside clicking noise, resembling a clockwork mechanism.

Results:: Oropharyngeal evaluation revealed rhythmic and brief contraction of posterior soft palate. Video-laryngoscopy recorded soft palatal lifting movements and myoclonic contractions of tensor veli palatini. EEG, multimodal evoked potentials, blink reflex study and 3T brain MRI were all unremarkable. Lack of inferior olive nuclei change signal or enlargement on MRI ruled out SPT [2]. Therefore, a diagnosis of EPT was made. The simultaneous 18F-FDG-PET/3T-MRI study showed an area of increased glucose uptake in the lower brainstem, nearby the inferior olive nuclei bilaterally, more on the right side.

Conclusions:: This is the first application of simultaneous 18F-FDG-PET/3T-MRI in EPT. Our results illustrate that lower brainstem encompassing the inferior olivary nuclei might be the underlying generator in case of EPT.
UNUSUAL CAUSE OF LATE-ONSET CHOREA: ERDHEIM CHESTER DISEASE

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Background and Aims: Erdheim-Chester disease (ECD) is a rare non-Langerhans cells histiocytosis. First described in 1930 by Jacob Erdheim and William Chester, till date since 1930 only 650 cases have been reported. Although tissue infiltration can occur in almost every organ, skeleton, retroperitoneum (mainly the kidney and aorta) and orbit involvement is common. Neurological involvement is seen in less than 50 % of patients. When patients have central nervous system involvement, they are often symptomatic, with diabetes insipidus and ataxia syndromes being the most common presentations.

Methods: A 60-year-old male presented with a history of insidious onset gradually progressive generalized choreo-athetoid movements since 6 years, cerebellar ataxia since 4 years. Detailed workup including genetic study was negative for inherited/genetic, structural, paraneoplastic, autoimmune, toxin/drug-induced, & metabolic causes of progressive choreoathetosis with the pan-cerebellar syndrome.

Results: MRI-brain showed pituitary macroadenoma, T2, & Flair hyperintensity in the midbrain, pons, & bilateral dentate nucleus. 18F-FDG-PET Scan showed, increased FDG activity in the midbrain, pons, pituitary fossa, in the superior mediastinum along the origin & proximal portion of left subclavian artery, perinephric soft tissue, bilateral renal sinuses, bilateral adrenal glands, along the wall of the aorta. Histopathology of the biopsy of perinephric soft tissue show CD68 positive aggregates of foamy macrophages, lymphocytes, plasma cells & eosinophils with areas of diffuse & dense fibrosis suggestive of ECD.

Conclusions: ECD is a rare cause of late-onset chorea. Only 3 cases have been reported who presented with chorea as the initial manifestation. A high degree of suspicion is required, PET CT can help in the diagnosis of ECD.
THE VIDEO HEAD IMPULSE TESTS IN THE PARKINSONIAN DISORDERS

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Background and Aims:: Recent studies have revealed significant abnormalities in the head-impulse test (HIT) in patients with cerebellar ataxia. We anticipated that the quantitative study of the VOR may help to detect cerebellar impairment in multiple systemic atrophy (MSA) and therefore to perform the differential diagnosis between idiopathic Parkinson’s disease (IPD) and other parkinsonian disorders.

Methods:: A retrospective analysis was performed in patients who presented with gait disturbance. The diagnosis of each parkinsonian disorder was based upon the clinical and laboratory data. The secondary parkinsonian disorders including normal pressure hydrocephalus and vascular parkinsonism were excluded. The VOR gain was calculated as the ratio between the integrated velocities of the eye relative to the head divided by the integrated velocities of the head during a time window from 0 to 20 ms after head impulse start.

Results:: A total of 77 patients with the primary parkinsonian disorders were included; IPD, MSA, and progressive supranuclear palsy. There were no statistically significant differences of age, MMSE score, and m-UPDRS motor score between disorders. The Kruskal-Wallis test showed that there was no significant difference of the VOR gain values and the gain asymmetry of each semicircular between the disorders. Pearson’s Chai-Square test showed that there was only a significantly higher occurrence rate of the CUS during vHITs in non-IPD patients than in IPD.

Conclusions:: These results suggest that the vHIT alone cannot discriminate between patients with primary parkinsonian disorders but only provide an ancillary information for distinguishing IPD from non-IPD.
MOTOR AND NON-MOTOR FLUCTUATIONS IN MEN AND WOMEN CITIZEN UZBEKISTAN WITH PARKINSON’S DISEASE

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Background and Aims:: To identify the frequency and characteristics of the motor and non-motor fluctuations in men and women with Parkinson's disease (PD) and to establish their impact on the quality of life of patients.

Methods:: We examined 42 men and 56 women with PD stages 2.5–4.0. The degree of clinical manifestations was determined using the Unified Parkinson's Disease Rating Scale and the Hoehn and Yahr scale. The 9-Symptom Questionnaire (patient self-assessment diary) was used to assess fluctuations. Quality of life was assessed using Parkinson's Disease Quality of Life Questionnaire 39 and the second part of the European Quality of Life Questionnaire.

Results:: Among motor fluctuations, the on-off phenomenon prevailed, which occurred in 69.8% of men and 73.7% of women. Vegetative fluctuations were observed in 86.0% of men and 93.0% of women. Certain autonomic disorders were found statistically significantly more often in women than in men. Mental fluctuations were found in 79.1% of men and 75.4% of women. Apathy was recorded statistically significantly more often in men than in women. Among sensory fluctuations observed in 55.8% of men and 50.9% of women, pain syndrome was statistically significantly more common in women.

Conclusions:: Gender influences the prevalence of certain non-motor fluctuations in PD patients.
THE ASSOCIATION OF COGNITIVE IMPAIRMENT AND OTHER NON-MOTOR SYMPTOMS AMONG THAI PARKINSON’S DISEASE PATIENTS

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Background and Aims:: Cognitive impairment is a common non-motor symptoms of Parkinson’s disease. This problem frequently impairs patients’ quality of life and cause disability to the patients. Our aims are to investigate the prevalence of cognitive impairment and the association of other non-motor symptoms in Parkinson’s Disease patients.

Methods:: Prospective cross-sectional study was carried in Chiang Mai University Hospital from November 2019 to June 2021. Data collection was done by data extraction checklist, Unified Parkinson’s Disease Rating Scale (UPDRS) examination and related questionnaires. The association between cognitive impairment and other non-motor symptoms was analyzed by multivariable logistic regression.

Results:: A total of 103 eligible Parkinson’s Disease patients were recruited during the study period. 49.5% of participants were male and mean age of all participants was 65.0 ± 9.4 years. Prevalence of cognitive impairment (defined by MoCA score Thai version < 26) and overall non-motor symptoms were 68.9% and 99.0% respectively. Non-motor symptom subtype of urinary symptoms was significantly associated cognitive impairment (aOR 8.42, 95%CI 1.32-53.87). For subitems of non-motor symptoms which significantly increased probability of cognitive impairment after adjustment were nocturia, unexplained weight change, anxiety, hallucination and salivary dribbling.

Conclusions:: This study emphasizes high prevalence of cognitive impairment and non-motor symptoms in Parkinson’s Disease patients. Parkinson’s Disease patient with problems of urinary symptoms especially nocturia, unexplained weight change, anxiety, hallucination or salivary dribbling should be screened for cognitive impairment.
ATYPICAL PARKINSONIAN SYNDROMES: ABOUT A SERIES OF 20 CASES

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CHU TIZI-OUZOU, Department Of Neurology, Chu Tizi Ouzou, Tizi-Ouzou, Algeria

Background and Aims:: The aim of this study was to define the clinical and radiological characteristics of patients presenting atypical PS, as well as their evolution under dopa therapy.

Methods:: This is a retrospective and observational study of 20 patients presenting atypical PS who had their follow up within the Neurology department in Tizi-Ouzou University Hospital (Algeria) over a period of 10 years (2009-2019).

The included Patients were diagnosed with MSA, PSP and CBD.

For each patient, we analysed the symptoms and clinical signs at the onset, brain MRI data and evolution under dopa therapy.

Results:: The most frequent occurrence was PSP (60%), followed by MSA (25%), contrary to the data in the literature (ref. 5), the average consultation time was short (one year), which we allowed a good appreciation of the input modes and the data of the initial examination. The mode of entry into MSA does not differ from the data in the literature; postural instability with falls and dysautonomia signs were almost constant (ref.1). The parkinsonian syndrome was variable depending on the pathology. In MSA, it was most often akineto-rigid in the limbs, atypical. In PSP, the axial site was predominant.

For dopa therapy, the beneficial effect was only observed in certain AMS, which is most often described (ref. 2). For suggestive radiological abnormalities; they are inconstant (ref. 5), which is the case in our patients.

Conclusions:: The differential diagnosis of parkinsonian syndromes remains a challenge for neurologists despite the improvement in clinical and pharmacological criteria and the development of visual analysis.
"PSEUDO INO" IN PROGRESSIVE SUPRANUCLEAR PALSY

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Background and Aims:: A 65 year old male, with 2 years presented with history of slowness of daily activities, occasional backward falls, apathy & behavioral complaints, and double vision.

Methods:: • Oculomotor findings were slow vertical and horizontal sacchades, supranuclear vertical > horizontal gaze paresis, bilateral lateral > medial gaze restriction with abduction nystagmus (not true INO, but INO-like) in presence of preserved convergence and bilateral VOR. No history of fatiguability, diminution of vision, cerebellar symptoms, autonomic symptoms. • Frontal assessment battery score 10/18 in form of subcortical frontal affection. Speech was hypophonic and slurred. Increased tone with Axial > Limb rigidity observed. Bilateral brisk DTR with mute plantar responses. Sensory examination was normal for all modalities. Cerebellar signs were absent, and patient had a slow, short stepped, extrapyramidal gait.

Results:: In our patient, a diagnosis of PSP was evident given the clinical scenario and MRI findings. • While True INO (caused by a MLF lesion) causes restricted medial gaze in ipsilateral eye, and corrective abduction nystagmus in other eye, our case had an Inter-nuclear ophthalmoparesis caused by unequal supranuclear denervation of lateral > medial recti causing diplopia as well as abduction nystagmus.
Conclusions:: • Previous descriptions of bilateral INO (WEBINO) and horizontal oculomotor findings in PSP have been published, however we present INO-like (Pseudo INO) disparity of intra-ocular horizontal movements (Lateral > Medial restriction) likely due to differential supranuclear denervation causing diplopia, and abduction nystagmus in presence of normal duction, convergence and bilateral VOR.
MANAGEMENT OF CRANIAL MOVEMENT DISORDERS WITH BOTULINUM TOXIN

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Background and Aims:: Botulinum toxin (BT) has truly revolutionized the management of movements disorders, although the marketing authorization is limited to cervical dystonia and blepharo-spasm. Its mechanism of action as well as its efficacy and tolerance profile allow recurrent use. Its use has grown considerably in recent years following the demonstration of remarkable efficacy in other indications, that we will discuss in this communication.

Methods:: Movement disorders that affect the neck, face, jaw, tongue or palate are a frequent neurological problem. These disorders can be limited to the cranial muscles or manifest as part of a more generalized movement disorder and Botulinum toxin is an effective symptomatic treatment in most focal cranial movement disorders. We will discuss through video clinical cases the management by Botulinum toxin of involuntary movements that affect the neck, face, jaw and tongue.

Results:: Clinical cases will be approached through videos to highlight clinical expression of cranial movement disorders before and after treatment, such as blepharospasm, eyelid apraxia, hemifacial spasm, face Tics, facial dyskinesia, synkinesis, cervical dystonia, head tremor, oromandibular dystonia, jaw tremor, edentulous dyskinesia, lingual dystonia and palatal tremor.

Conclusions:: Considerable advances have been made in the past two decades, but we still need to improve our knowledge of the diagnosis and treatment of cranial movement disorders. The clinical characteristics seem to be well delineated; however, the differential diagnosis and management of these disorders can be complex owing to the similarities in patterns of muscle involvement and activation profiles in different disorders.
EMG-GUIDED INJECTION OF BOTULINUM TOXIN A IN THE TREATMENT OF PISA SYNDROME: A CASE REPORT OF A TAILORED MULTILEVEL APPROACH

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Background and Aims:: Pisa syndrome (PS) is a disabling, medication-resistant, postural abnormality that may affect 7-10% of patients with Parkinson's disease (PD). In this case report, we evaluate the efficacy of botulinum toxin Electromyography-guided injections in PD-associated PS using a tailored multilevel approach.

Methods:: We describe the case of a 72-year-old man with diagnosis of PD with a severe axial-lateral flexion of the trunk to the left side. Surface Electromyography (SEMG) bilateral recordings of paraspinal muscles, latissimus dorsi, levator scapulae and obliqui externi were performed in walking and sitting posture. Right paraspinal muscles T7-T8 showed a pattern of continuous muscle activity. We decided to treat with incoBTX-A these hyperactive muscles. After incoBTX-A injections, the patient was involved in a customized rehabilitation program to improve the muscle activity of the left side: exercises were identified using SEMG recordings. After 6 months, SEMG evaluation revealed a pattern of hyperactivity of the T10-T11 paraspinal muscles which were treated with incoBTX-A. The patient was evaluated at baseline, at 6 and 12 months, measuring the angle of trunk inclination in standing position using a goniometer.

Results:: At 6 and 12 months after the beginning of combined treatment, the patient showed an improvement of 10° angle of trunk inclination. The procedure was well tolerated, without side effects or complications.

Conclusions:: These results suggested that a tailored multilevel approach using botulinum toxin injections combined with a rehabilitation program could be a useful therapeutic strategy for PD subjects with PS for improving axial posture and trunk mobility.
MOVEMENT SMOOTHNESS IMPAIRMENT IN IDIOPATHIC CERVICAL DYSTONIA

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Background and Aims:: Voluntary movement is characterized by accuracy, speed and smoothness. Although phenomenology of idiopathic cervical dystonia (ICD) is typically defined by abnormal postures (with head deviation at rest) plus dystonic twisting or tremulous movements, also head voluntary movements and motor control can be impaired. This complex impairment leads to disability in peripersonal space exploration in daily life activities. The current work is aimed at evaluating if smoothness of voluntary head rotations is reduced in ICD.

Methods:: Participants (18 ICD patients with torticollis and 18 controls) completed discrete rightward and leftward head rotations in an optoelectronic movement analysis laboratory (Smart D, BTS, Italy). Patients head movements were analyzed in the case of the rotation in the opposite direction to the torticollis (AwayDys). Amplitude and angular velocity were measured and indices from angular jerk and the arc length of the spectrum of the angular speed (i.e. SPARC, arbitrary units) were chosen as smoothness measures (the higher, the smoother). Generalised linear mixed effects models were used for statistics.

Results:: Controls’ movements (49.2 °/s, 41.9-56.9 °/s) were faster than AwayDys (28.9 °/s, 22.9-35.5 °/s). Net of any difference in amplitude and speed, SPARC (but not jerk) showed reduced smoothness in patients’ AwayDys (1.46, 1.35-1.61) compared to controls (1.86, 1.72-2.03).

Conclusions:: Poor smoothness is an independent and clinically relevant motor disturbance in ICD. SPARC is a valid measure of movement smoothness to differentiate HC and ICD patients and possibly a synthetic index in monitoring treatments like botulinum neurotoxin injections and adjunct motor learning programs.
CREUTZEL-JAKOB DISEASE MIMICS A RICHARDSON SYNDROME, SPECTRUM OF SUPRANUCLEAR PROGRESSIVE PALSY

Background and Aims:: The clinical spectrum of Creutzfeld-Jakob disease (CJD) is extensive. CJD in the sporadic variant could be debut as prominent ataxic (10%) or thalamic (2%) of cases) symptoms. In a patient with rapidly cognitive impairment in less than six months, the probability of diagnosis is high. We presented a man with six months of evolution con cerebellar syndrome, ocular supraversion limited and symmetrical parkinsonism with multiple cognitive impairments that simulated a Richardson spectrum of Supranuclear progressive Palsy.

Methods:: March 2020
The patient initially presented extreme behavioural changes, obsessive-compulsive, alterations in the sleep pattern (parasomnias), in addition to only sleeping five hours a day, irritability, frequent mood changes, feelings of hopelessness and anxiety were observed. October 2020
Weight loss of 13 kg in four months. January 2021, he starts impairment in episodic, working and semantic memory. Errors in the execution, planning, and sequence of previously learned actions were typical. February 2021
He presented insidiously with gait disturbance consisting of indistinct lateropulsion and a broad base of support. Alterations in eye movements due to patient's inability to fix the gaze in the horizontal and vertical plane), intention tremor, changes in the voice (fluency has become slow, he drags the words and tends to separate in syllables).

Results::
Ocular movements
Gait
### Conclusions:: Table 1.

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<tr>
<th>Lumbar puncture</th>
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<tr>
<td>pH 7.72</td>
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<td>Proteins 57.2 mg/dl</td>
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<td>Cells 12</td>
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<td>Glucose 62 mg/dl</td>
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<td>14-3 protein 80,000 (0-20,000) UA/ml</td>
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<td>Beta-amiloid 621 pg/ml</td>
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A sporadic CDJ was made. A hockey stick sign was observed in the cranial MRI.
MESENCHYMAL STEM CELL THERAPY FOR PARKINSON'S DISEASE: SYMPTOMS DURING THE SIX MONTHS POST-TRANSPLANT PERIOD COMPARED WITH PLACEBO

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Background and Aims:: Treatment of patients with Parkinson disease (PD) using autologous mesenchymal stem cells (MSCs) is a promising method to influence the pathogenesis of the disease. However, this method of PD treatment isn't a fully understood process and requires a long follow-up in the post-transplant period and assessment of the possible placebo effect on the recovery process. Our study has started in January 2019 and now included 22 PD patients in the post-transplant period and 13 PD patients that received placebo. The aim was to assess the results of the introduction of MSCs and placebo on the dynamics of motor and non-motor symptoms during the six months post-transplant period.

Methods:: MSCs were transplanted to 22 patients with PD intravenous and tandem (intranasal + intravenous) injections. Placebo therapy (isotonic saline) was performed to 13 patients with PD via tandem injection. Effectiveness of the therapy was evaluated 7 days, one, three and six months post-transplantation according to the dynamics of non-motor symptoms by scoring the following scales: Hamilton Depression Rating Scale, The Pittsburgh Sleep Quality Index, Non-Motor Symptoms Scale, The 39-item Parkinson's Disease Questionnaire. The severity of motor symptoms was evaluated on the basis of Section III of the Unified Parkinson's Disease Rating Scale.

Results:: The severity of motor and non-motor symptoms in the post-transplant period decreased in contrast to the control group.

Conclusions:: Our results of the introduction of MSCs on the intensiveness of the motor and non-motor symptoms exceed the placebo effect and allow us to consider MSCs transplantation as a disease-modifying therapeutic strategy in PD.
TWO DISTINCT AND CONSECUTIVE BRAINSTEM DEMYELINATING LESIONS POST-IRRADIATION OF CRANIAL NERVE SCHWANNOMA: WHICH DIAGNOSIS?

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Background and Aims:: Demyelination is a known neurological side effect of radiation therapy (RT). Moreover, radiation has been discussed as a potential causative factor for Multiple Sclerosis (MS). We report the case of a 38-year-old female radio-treated for right jugular foramen schwannoma, after which she developed two consecutive symptomatic brainstem demyelinating lesions.

Methods:: MRI were recorded at the admission and during hospitalization. CSF analysis was performed.

Results:: 5 months after RT, the patient developed a right medulla T2-Flair hyperintense lesion, with moderate contrast-enhancing, symptomatic for controlateral brachio-crural sensitive-motor syndrome, ipsilateral deviation of the tongue and dysphagia. Supposing a post-irradiation neurotoxicity, she was treated with oral corticosteroids for 3 months; complete remission followed. Seven months later, she developed diplopia and headache, with appearance of a similar lesion in right pons-peduncular cerebellum on MRI. Medullary MRI was negative, CSF analysis showed mononuclear pleocytosis and presence of liquoral oligoclonal bands, differential diagnostics tests for other demielinating syndromes including anti-MOG and AQP-4 Ab were negative. She was treated with high-dose steroids i.v. with initial clinical and radiological improvement. Follow-up is ongoing.
Conclusions: It has been suggested that RT could alter the nervous tissue in radiation clinical target volume, making it vulnerable to a pre-existing autoimmune attack predisposition. Even if only few cases of MS following RT have been reported so far, this case underlies that caution should be used in patients with demyelinating lesions post-RT, especially young women with relapsing course, keeping in mind the differential diagnoses in order to avoid mistakes or treatment delays.
LONG-TERM EFFICACY AND SAFETY OF ECULIZUMAB IN AQUAPORIN-4 IMMUNOGLOBULIN G-POSITIVE NEUROMYELITIS OPTICA SPECTRUM DISORDER

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Background and Aims:: In PREVENT, eculizumab reduced relapse risk in patients with aquaporin-4 immunoglobulin G-positive (AQP4+) NMOSD by 94.2% vs placebo. We present the long-term efficacy and safety data from PREVENT (NCT01892345) and its open-label extension (OLE; NCT02003144). Eculizumab is not reimbursed for neurology indications in Italy as of April 2021.

Methods:: During PREVENT, adults with AQP4+ NMOSD received eculizumab or placebo with/without immunosuppressive therapy (IST), after which, patients could receive eculizumab in the OLE. Eculizumab data from PREVENT and its OLE were combined for this analysis.

Results:: Overall, 137 patients received eculizumab for a total of 362.3 patient-years. At 192 weeks, 94.4% (95% CI: 88.6–97.3%) of patients were relapse free. The adjudicated annualised relapse rate was 0.025 (95% CI: 0.013–0.048); the annualised relapse-related hospitalisation rate (ARRHR) was 0.03/patient-year (95% CI: 0.017–0.055). Rates of AEs and serious AEs (SAEs)/100 patient-years were 732.5 and 33.7, respectively. Common SAEs, excluding NMOSD relapses, were pneumonia (3.6%), urinary tract infection (2.9%) and acute cholecystitis (2.9%). One patient died (pulmonary empyema) and one developed disseminated Neisseria gonorrhoeae infection. Overall, 25/137 patients (18.2%) developed a serious infection vs 6/47 (12.8%) receiving placebo (none meningococcal). During the OLE 42% of patients changed IST; most (88%) stopped or decreased IST use.

Conclusions:: The proportion of relapse-free patients remained high (94%) through 192 weeks. Eculizumab was well tolerated and AEs were consistent with the established safety profile. ARRHR was low and most patients reduced or stopped concomitant IST. This study was funded by Alexion Pharmaceuticals, Inc.
CONSTRUCTION OF A RESOURCE FOR ADVANCE CARE PLANNING IN MULTIPLE SCLEROSIS (CONCURE-SM): RESULTS OF COGNITIVE DEBRIEFING WITH USERS

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Background and Aims:: ConCure-SM is a mixed-methods research project for developing and testing an advance care planning (ACP) intervention for people with progressive multiple sclerosis (pwPMS) in Italy. It consists of a booklet to be used during the ACP conversation (the focus of this presentation) and a training program for MS healthcare professionals (HPs). Aims: To assess the acceptability and comprehensibility of the ConCure-SM booklet.

Methods:: An interdisciplinary panel translated and adapted to the Italian legislation and to the MS context a booklet developed by the National ACP programme for New Zealand. The booklet was then probed via individual cognitive interviews with pwPMS and caregivers, and a focus group meeting (FGM) with MS HPs.

Results:: We conducted 13 interviews (September-January 2021) which lasted between 36 and 80 minutes. Participants were 10 pwPMS and 3 caregivers; 8 were men, median age was 54 years. Twelve HPs participated in the FGM (7 neurologists, 3 psychologists, one nurse and one physiotherapist), which lasted 105 min. Thematic analysis identified 4 overarching themes: comprehensibility and clarity; content acceptability and emotional impact; images and layout; suggestions for improvement. Interviews revealed that the booklet was useful and informative, though pwPMS found it emotionally taxing. The FGM was well participated; few experiential data on ACP emerged, lack of training and time constraint emerging as major reasons.

Conclusions:: Cognitive debriefing was key to refine the ConCure-SM booklet. Interview and FGM results corroborated use of the booklet within the ACP conversation, and the challenge of appraisal as a stand-alone tool.
CLINICAL RELEVANCE OF MULTIPARAMETRIC MRI ASSESSMENT OF CEREBELLAR DAMAGE IN MULTIPLE SCLEROSIS

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\textbf{Background and Aims::} To quantify in-vivo cerebellar damage and identify MRI predictors of physical disability and cognitive dysfunction in multiple sclerosis (MS) patients, and to characterize patients with cerebellar disability in terms of MRI findings.

\textbf{Methods::} One-hundred and sixty-four (89 relapsing-remitting and 75 progressive) MS patients and 53 healthy controls underwent brain and cervical cord 3Tesla MRI with sequences for assessing lesions and atrophy in brain and cervical cord, and diffusion-tensor metrics of cerebellar peduncles. Subjects underwent neurological examination and neuropsychological assessment. MRI predictors of clinical variables were identified with random forest models. Hierarchical clustering was applied on MRI metrics in patients with cerebellar disability.

\textbf{Results::} In MS patients, informative predictors were lower cord grey matter (GM) area, higher cord GM lesion volume (LV), lower brain volume, lower brain GM volume (GMV), higher brainstem LV, lower cord global area, lower brain cortical GMV, lower cerebellum lobules I-IV and vermis GMV for higher Expanded Disability Status Scale score (out-of-bag-R\textsuperscript{2}=0.83); higher supratentorial and superior cerebellar peduncle LV, lower brain volume, lower thalamus volume, lower cerebellum lobule VIIIb GMV, lower basal ganglia volume, lower brain GMV and lower cerebellum Crus II GMV for lower cognition z-score (out-of-bag-R\textsuperscript{2}=0.25). In patients with cerebellar disability, we found three MRI-clusters: high brain LV (including cerebellar peduncles), marked cerebellum GM atrophy, and severe cord damage.

\textbf{Conclusions::} Damage to cerebellum GM and connecting structures has a relevant role in explaining cognitive dysfunction and physical disability in MS. The identification of three MRI-subtypes of patients with cerebellar disability is a step forward in MRI-clinical correlations.
REVEALING STRUCTURAL AND CLINICAL HETEROGENEITY IN THE SPECTRUM OF NEUROMYELITIS OPTICA WITH UNSUPERVISED MACHINE LEARNING

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Background and Aims:: The spectrum of neuromyelitis optica (NMOSD) includes different phenotypes and serotypes. Understanding disease heterogeneity is fundamental for targeted treatment. We aimed to unravel differences among NMOSD patients using unsupervised machine learning.

Methods:: We obtained MR images and clinical data from 140 patients with NMOSD (n=105, 88 aquaporin-4-IgG [AQP4]-positive, 17 AQP4-negative) or AQP4-negative NMOSD-like manifestations (n=35, 17 recurrent myelitis [RM] and 18 recurrent optic neuritis [RON]) and 151 healthy controls. CNS damage (brain, optic nerve [ON] and cervical cord) was assessed in terms of lesions, normalized volumes, and cortical thickness. We computed between-group differences with age-, sex- and site-adjusted linear models. Based on structural measures, we ran unsupervised clustering analysis among NMOSD/NMOSD-like patients.

Results:: Except for RM, NMOSD and NMOSD-like patients had diffused cortical atrophy (p<0.008), which was worse in the cingulate (AQP4-positive NMOSD, p=0.001), parietal (AQP4-negative NMOSD, p=0.008) and occipital lobes (RON, p=0.022). AQP4-positive NMOSD had reduced normalized brain volume (p<0.006) and cervical cross-sectional area (p=0.02). AQP4-negative NMOSD and RON had ON atrophy (p<0.03), the latter with additional optic chiasm atrophy (p<0.001). Clustering analysis identified three groups of NMOSD/NMOSD-like patients, with similar ON and cord lesion volume/length, number of optic neuritis/myelitis and phenotypes. Cluster-1 included patients with higher brain lesion volume (p<0.048), cluster-2 included patients with worse ON and cord atrophy (p<0.048) and cluster-3 included patients with greater cortical atrophy, milder disability, and higher rate of oligoclonal bands (p<0.037).

Conclusions:: The heterogeneity of NMOSD spectrum goes beyond clinical manifestations and serostatus, possibly mirroring different pathophysiological substrates.
DYNAMIC FUNCTIONAL CONNECTIVITY ANALYSIS IN THALAMIC SUB-REGIONS SHOWS DIVERGENT PATTERNS IN MULTIPLE SCLEROSIS PHENOTYPES

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Background and Aims:: In multiple sclerosis (MS), thalamic sub-regions (frontal, motor, occipital, post-central and temporal) show distinct resting state (RS) functional connectivity (FC) abnormalities. Besides RS FC, thalamus also showed dynamic FC (dFC) abnormalities in MS. Here, we explored sub-regional thalamic dFC in MS.

Methods:: Eighty-nine MS patients (49 relapsing-remitting [RR]; 40 progressive [P]MS) and 53 healthy controls (HCs) performed RS fMRI, clinical and neuropsychological assessment. Thalamic sub-regional dFC was calculated as the standard deviation of FC assessed through sliding-window seed-voxel analysis. Between-group comparisons and correlations were assessed with voxel-wise ANOVA, t-Tests and linear regressions.

Results:: MS patients, especially RRMS, showed a lower dFC between most of thalamic sub-regions and fronto-temporo-occipital areas vs HCs. In addition, PMS also displayed higher dFC vs HCs and RRMS between posterior thalamic sub-regions and occipito-parietal cortices and basal ganglia. Cognitive impairment was associated with higher dFC between motor, temporal and occipital thalamic sub-regions and cortical areas belonging to the sensorimotor and default-mode networks. Higher clinical disability was associated with lower dFC between post-central thalamic sub-regions and frontal cortex in RRMS and with higher dFC between post-central and left frontal thalamic sub-region and left occipital/right insular cortices in PMS.

Conclusions:: RRMS patients experienced reduced dFC vs HCs. On the other hand, PMS patients and patients with more severe clinical and cognitive disability also displayed higher thalamo-cortical dFC. Higher dFC may reflect adaptive mechanism at early stages and maladaptive mechanisms at later stages of the disease. Funding: Antonio Carotenuto is supported by a MAGNIMS/ECTRIMS research fellowship.
MICROCHIMERISM IN MULTIPLE SCLEROSIS: THE IMPACT OF SEX-RELATED DIFFERENCES IN FETAL-MATERNAL CROSS-TALK ON THE CLINICAL AND RADIOLOGICAL PHENOTYPE IN WOMEN WITH MULTIPLE SCLEROSIS

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Background and Aims:: Multiple Sclerosis (MS) is a chronic autoimmune disorder characterised by inflammation and neurodegeneration. Persisting fetal microchimeric cells seem to contribute to autoimmune diseases pathogenesis. The aim of the study is to investigate the impact of microchimerism on the clinical, radiological, and laboratory features of MS.

Methods:: We recruited 101 consecutive MS patients: 43 nulliparous subjects (age: 36.1 ± 9.5, disease duration: 10.4 ± 8.7, median EDSS: 2.5), 40 patients with at least one male son (age: 42.3 ± 10.0, disease duration: 11.4 ± 8.5, median EDSS: 2.5), and 18 patients with only daughters (age: 47.2 ± 10.5, disease duration: 17.6 ± 12.6, median EDSS: 3.75). Demographic, clinical, radiological, and paraclinical data at baseline and follow-up were collected. MRI protocol included 3D-T2w FLAIR FatSat and 3D-T1w FSPGR.

Results:: Patients with at least a male son had a significantly higher age at onset (p<0.001) and a highest frequency of pyramidal onset (p<0.001). The same group had a shorter time-gap from onset to EDSS 4 and to EDSS 6 when compared with the group with only female daughters (respectively, 113.4 ± 17.5 vs 201.7 ± 44.3, p=0.039; 98.8 ± 25.2 vs 203.2 ± 49.4, p=0.058). Finally, patients with at least a male son had a lower chiasm volume when compared with the nulliparous patients (p=0.023) and with the only-daughter group (p=0.019).

Conclusions:: In a multifactorial background, the microchimeric XY fetal cells could modulate the inflammatory and neurodegenerative mechanisms underlying the MS, influencing the disease features.
DEVELOPMENT OF AN APP (ABOUTCOME) FOR EVALUATION IN MULTIPLE SCLEROSIS

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Background and Aims:: Data collection represents fundamental component of clinical research and practice, allowing analysis of collected data. The aim of the study is to implement data collection through creation and validation of the app ABOUTCOME, to allow data storage and facilitate patients to fulfil questionnaires.

Methods:: ABOUTCOME has been developed for people with Multiple Sclerosis (PwMS). It consists of standardized tests and self-administered measures. Measures included: Disability of the Arm Shoulder and Hand (DASH), Abilhand, Manual Ability Measure-36 (MAM-36), Fatigue Severity Scale (FSS), Modified Fatigue Impact Scale (MFIS), Modified Ashworth Scale (MAS), 9-Hole Peg Test (9-HPT), Hand Grip Strength (HGS), Expanded Disability Status Scale (EDSS), Brief International Cognitive Assessment Multiple Sclerosis (BICAMS). ABOUTCOME is multilanguage (Italian and English), with available users’ manual.

Results:: 16 PwMS [10 female, mean age 58.2 years (DS=7.71), mean EDSS 6.5 (DS=0.98), 3 relapsing remitting MS, 13 progressive MS] completed 5 self-administrated scales (DASH, Abilhand, MAM-36, FSS, MFIS) on paper and tablet version. An ad hoc questionnaire has been created to evaluate necessary commitment to complete questionnaires, mental fatigue and frustration level due to paper and tablet implementation.

Conclusions:: 14 MS subjects preferred and considered less challenging tablet compilation. The possibility to use a simple finger tap rather than pencil pinch has proved to be good alternative, reducing subjects effort and time employed. Data export and database creation directly from ABOUTCOME resulted easier and more immediate, removing paper transcription errors. ABOUTCOME is available on Android systems and can be implemented including other evaluation measures.
VITAMIN D LEVELS INFLUENCE RADIOLOGICAL AND LABORATORY OUTCOMES OF MULTIPLE SCLEROSIS PATIENTS TREATED WITH OCRELIZUMAB

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Background and Aims:: Several observational studies showed an association between low circulating levels of 25-hydroxy-vitamin D (25-OH-VitD) and an increase of inflammatory activity in Multiple Sclerosis (MS). The aim of our study is to evaluate disease activity and CD19 kinetic in Ocrelizumab-treated MS patients, and their associations with 25-OH-VitD levels.

Methods:: Retrospectively collected data on new T2 or Gd+ lesions at magnetic resonance imaging (MRI), and laboratory measures including 25-hydroxy-vitamin D levels. According to CD 19 B lymphocytes count after 6 months of treatment (cut-off: <0,1%), patients were divided into two groups: with fast (FR) and slow (SR) repopulation rate. The independent samples t-test and Spearman correlation coefficient were used to test differences between means and association between 25-OH-VitD levels, radiological outcomes, and laboratory measures.

Results:: 94 MS patients with a mean follow-up of 14 months were enrolled. On MRI, new T2 and/or Gd+ lesions were seen in 11,8 % (12 out of 101 scans). Seasonally adjusted 25-OH-VitD levels in samples drawn close to all magnetic resonance images with new T2 and/or Gd+ lesions were lower compared to the remainder (18,72 vs. 31,71 ng/ml; p = 0.0367). Moreover, the FR rate group showed lower levels of 25-hydroxy-vitamin D compared to LR group (19,74 ng/ml vs. 29,42 ng/ml p = 0,0142). Levels of 25-hydroxy-vitamin D were associated with CD19 cells number at 6 months(r² = -0.5449; p = 0.0013).

Conclusions:: Higher 25-OH-VitD levels were associated with LR rate and better radiological outcomes.
NODDI MICROSTRUCTURAL ABNORMALITIES IN NORMAL-APPEARING GRAY MATTER AND WHITE MATTER CONTRIBUTE TO COGNITIVE IMPAIRMENT IN MULTIPLE SCLEROSIS

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Background and Aims:: Heterogeneous processes contribute to multiple sclerosis (MS)-related cognitive impairment. Using neurite orientation dispersion and density imaging (NODDI), we explored the associations between microarchitecture abnormalities of focal lesions and normal-appearing (NA) tissues and cognitive impairment in patients with MS (PwMS).

Methods:: One hundred and fifty-two PwMS and 48 healthy controls (HC) underwent a brain 3T acquisition. PwMS with ≥1 abnormal test in ≥2 domains of Rao’s battery were defined as cognitively impaired (CI). A cognitive impairment index (CII) was also derived. NODDI-derived intracellular (ICV_f) and extracellular volume fractions (ECV_f) and orientation dispersion index (ODI) were assessed in cortical and white matter (WM) lesions, thalamus, NA-cortex and NAWM.

Results:: Fifty-two (34.2%) PwMS were CI. CI and cognitively preserved (CP) PwMS vs HC showed significantly decreased NA-cortex, thalamic and NAWM-ICV_f (p<0.001) and NA-cortex-ODI, and increased NAWM-ECV_f (p<0.003). CI PwMS showed also a significantly decreased thalamic-ODI and increased NAWM-ODI (p<0.018). CI vs CP PwMS had significantly decreased NA-cortex-, thalamic- and NAWM-ICV_f and thalamic-ECV_f, and increased NAWM-ECV_f and ODI (p<0.016). No lesional microstructural differences were found in CI vs CP PwMS. NA-cortex-ICV_f and NAWM-ICV_f and ODI were significantly correlated with CII (r from -0.24 to 0.30 p from 0.006 to 0.047).

Conclusions:: NA-cortex, thalamic and NAWM neuro-axonal loss, together with NAWM inflammation, gliosis and loss of tissue coherence, are associated with cognitive impairment in MS. NODDI could disentangle in vivo the complex processes determining cognitive dysfunctions. Funding: This study was partially supported by Fondazione Italiana Sclerosi Multipla (fellowship: FISM2019/BS/009 and grant: FISM2018/R/16).
PREDICTORS OF OCRELIZUMAB EFFECTIVENESS IN PATIENTS WITH MULTIPLE SCLEROSIS

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Background and Aims:: We aim to provide effectiveness and safety data of ocrelizumab in patients with relapsing-remitting (RR-) and progressive multiple sclerosis (P-MS) and to evaluate clinical and immunological predictors of early treatment response.

Methods:: Demographic characteristics, effectiveness outcomes (time-to-confirmed disability worsening, time-to-first relapse, time-to-first evidence of MRI activity and time-to-first evidence of disease activity), clinical and immunological predictors of early treatment response and incidence of adverse events (AEs) were recorded at baseline and throughout follow-up (FU).

Results:: 153 subjects were included [93 RR-MS, 43 primary-P-MS (PP-MS), 17 secondary-P-MS (SP-MS); 60% females; baseline mean(SD) age 41.9(11.4) years; mean(SD) disease duration 10.3(9.9) years; mean(SD) annualized relapse rate 0.5(0.7); median(IQR) EDSS 3.5(2-5.5)]. At 2 years, disability worsening-free survival was 90.5%, 64.7% and 68.8% for RR-MS, PP-MS and SP-MS patients, respectively. At 2 years, 67.1%, 72.7% and 81.3% of patients with RR-MS, PP-MS and SP-MS were free of MRI activity, with NEDA-3 percentages of 62.1%, 54.6% and 55.1%, respectively. A lower baseline EDSS was independently associated with reduced risk of disability worsening HR(95%CI)=1.45(1.05-2.00), p=0.024, while previous treatment exposure with increased probabilities of radiological activity [HR=2.53(1.05-6.10), p=0.039]. At 6 months, CD8+ cell decrease was less pronounced in patients with inflammatory activity (p=0.022). Upper respiratory tract infections were the most frequently AEs.

Conclusions:: Ocrelizumab is a good treatment option in RR-MS and P-MS patients, with a manageable safety profile. Better outcomes were observed in treatment-naive patients and in patients with a low baseline disability. Depletion of CD8+ cells could underlie early therapeutic effects of ocrelizumab.
**FIRST-LINE THERAPIES IN LATE ONSET MULTIPLE SCLEROSIS: AN ITALIAN REGISTRY STUDY**

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**Background and Aims:** Late-onset (≥50 years) relapsing remitting Multiple Sclerosis (LORRMS) is associated with adverse prognosis but established marker(s) of such poor prognosis are still lacking in the clinical practice. The aim of the study is to compare effectiveness of injectable and oral first line disease modifying therapies (DMTs) in a cohort of patients with LORRMS for time to first relapse, time to confirmed disability progression (CDP), and, additionally, for time to discontinuation.

**Methods:** This is a multicenter, observational, retrospectively acquired cohort study on LORRMS-naïve patients from the Italian MS Register who started either injectable or oral first line DMTs between January 1, 2013 and December 31, 2017. LORRMS were divided into two groups, namely the injectable group (IG) and oral group (OG). Cox models adjusted with inverse probability weighted propensity score were built for the investigated outcomes.

**Results:** Of a cohort of 3,989 patients, 302 were enrolled (203 in the IG and 99 in the OG). The two cohort did not differ for baseline characteristics. Time to first relapse did not show any difference between the two groups (HR = 1.10; CI 95% 0.50-2.46, p=.797). Furthermore, no differences were found between the two groups with respect to the risk of CDP (HR = 1.04; CI 95% 0.35-3.06, p = .939), nor for the risk of DMT discontinuation (HR = 0.90; CI 95% 0.17-2.08, p = .425).

**Conclusions:** Real-world data from the Italian MS Register suggested that both injectables and oral first line DMTs controlled similarly the investigated outcomes in LORRMS.
EMOTION AND MULTIPLE SCLEROSIS: A FUNCTIONAL TRANSCRANIAL DOPPLER STUDY

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Background and Aims:: Multiple sclerosis (MS) manifests itself mostly as white matter demyelination and associated axonal damage. Emotional and mood changes are very frequent in MS patients. However, recent studies indicate that the MS patients show signs of impaired emotional reactivity. The aim of the study was to investigate the neuropsychology of emotions in MS patients by transcranial Doppler ultrasonography.

Methods:: For this reason, blood flow velocity changes were investigated in both middle cerebral arteries during a rest condition and when viewing non-emotional and emotional slide sequences. The study included 19 MS patients and 20 healthy subjects.

Results:: The negative emotional task was accompanied by a significantly higher increase in the right than in the left MCA in the control group alone. MS patients showed a bilateral, symmetrical increase in MFV. To determine whether there was a dysfunction in cerebrovascular reactivity and a deficit in the ability to activate both hemispheres in response to non-emotion-related stimuli in MS patients, the protocol study included a cerebrovascular reactivity test to apnea, a motor task and a cognitive task performed by both patients and controls. The pattern of MFV changes during these tasks was not statistically different in experimental groups.

Conclusions:: This study shows the possibility of obtaining specific functional information by means of bilateral transcranial Doppler ultrasonography and suggests a emotional processing deficit in MS patients. This finding points to a disruption of the neural circuits that link the prefrontal, posterior parietal, superior temporal and limbic cortices to subcortical structures in MS patients, as well as a possible interhemispheric disconnection.
IDENTIFY UNANSWERED QUESTIONS IN MULTIPLE SCLEROSIS. A COCHRANE STRATEGY TO PRIORITIZE FUTURE RESEARCH.

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Background and Aims: In an ever-increasing world of scientific knowledge, capabilities, and expectations, the extent of uncertainty is rarely discussed. Identifying, not neglecting, unanswered questions in medicine can enable research to determine which questions matter most, thus deserving priority attention. Since 2006, Cochrane has progressively implemented prioritization mechanisms for key review topics, now within the “Cochrane Methods priority setting Group”. Cochrane Groups in neurology field launched their priority setting exercises with the aim of identifying pressing questions to make sure that neurological systematic reviews will be as useful as possible to the people who need them. Recently Cochrane Multiple Sclerosis Group, in collaboration with Cochrane Neurological Sciences Field, decided to start an international consultation process aimed at identifying five new topics for upcoming Cochrane reviews on MS.

Methods: An online survey, translated in 12 languages, was run asking respondents (researchers, clinicians, patients and carers) to identify and rank 5, out of 16, high priority questions of potential uncertainty in five core areas (diagnosis, health communication and participation, pharmacological treatments, rehabilitation and social support interventions), selected by members of a Steering Group made up of different stakeholders. Participants could add an additional free-text priority research topic.

Results: 1372 participants from 50 countries prioritized the following: Magnetic Resonance Imaging in predicting disability worsening, comparison of benefits and harms of disease modifying drugs, psychological health, role of multidisciplinary care teams, benefits and harms of exercise.

Conclusions: Top priorities for the future research agenda in Multiple Sclerosis have been identified by equal partners with different perspectives and cultural viewpoints.
EVALUATION OF A COOLING VEST DESIGNED FOR DAILY USE IN IMPROVING PHYSICAL PERFORMANCE OF MULTIPLE SCLEROSIS PATIENTS

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Background and Aims:: Fatigue is a common symptom in Multiple Sclerosis (MS) and has a significant impact on patients’ life. This disabling condition and other symptoms are often worsened by high environmental temperature and increase of body temperature (e.g. during physical exercise) limiting patients’ physical activity. In order to improve the quality of life of PwMS (patients with MS), a wide range of cooling methods were tested, all of which showed to improve physical endurance and to prevent symptoms worsening. Aim of this study is to evaluate the efficacy of a cooling vest specifically designed for patients’ daily use.

Methods:: A cross-over study was conducted in a group of PwMS comparing their physical performance (distance and walking time to exhaustion) while wearing the cooling vest and in normal condition. As secondary outcomes heart rate, thermal sensation, skin back, and chest temperature were considered.

Results:: Ten patients were recruited. While wearing the vest, patients walked farther (1879±539m vs 1302±318m, p<0.001) and longer (1896±602s vs 1399±404s, p<0.001). At the end of the test, skin back and chest temperature were lower (-3.9±1.8 °C, p=0.001 and -2.7±1.8 °C, p<0.01 respectively), while no difference was observed for heart rate and thermal sensation.

Conclusions:: Studied cooling vest demonstrated to increase physical performance of PwMS. More studies on this topic are needed, but this preliminary result shows a possible way to improve patients' daily quality of life.
MULTIMORBIDITY IN MULTIPLE SCLEROSIS: IMPACT ON DISABILITY, QUALITY OF LIFE AND HEALTH STATUS

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Background and Aims: Multiple Sclerosis (MS) can be associated to different comorbidities, and presence of multimorbidity (i.e. the joint presence of two or more condition in addition to MS) may impact on hospitalization, relapse and mortality. Little is known on multimorbidity impact on disability, quality of life and general health status in MS.

Methods: We consecutively enrolled MS patients and addressed multimorbidity with the Structured Comorbidity Questionnaire (SCQ). Measures of disability, QoL, anxiety, depression and cognitive functioning were also administered.

Results: A total of 151 patients (93 females, average age 51.6±5.8, average EDSS 2.6±1.6) were enrolled, and 77 of them (51%) scored positively for multimorbidity. Multimorbidity was associated to higher disability and lower QoL (both p<.001), higher symptoms of depression (p=.004), higher state and trait anxiety levels (p=.003 and p=.013, respectively). No differences were found for age, disease duration, EDSS, progressive course and cognitive functioning. In a multivariable regression model, depression, trait anxiety and SCQ score predicted both disability (R2=.524) and QoL (R2=.411) variation.

Conclusions: More than half of MS patients herein enrolled had multimorbidity according to the SCQ, and showed worse disability, QoL, anxiety and depression. Moreover, disability and QoL were predicted by depression, trait anxiety and SCQ score. Identification and treatment of common mental health symptoms, such as depression and anxiety, might positively impact on disability and QoL improvement.
Multiple Sclerosis Functional Composite Predicts Thalamic Atrophy in Multiple Sclerosis

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Background and Aims:: In people with multiple sclerosis (pwMS) thalamic atrophy is strongly associated with cognitive functions while inconsistent results have been shown with the expanded disability status scale (EDSS). This might depend on the fact that EDSS is too much weighted for motor deficits. To overcome these EDSS limitations, it was developed the Multiple Sclerosis Functional Composite (MSFC) which includes the assessment of: i) leg function (Timed 25-Foot Walk/T25FT), ii) arm function (9-Hole Peg Test/9-HPT), iii) attention (Paced Auditory Serial Addition test/PASAT). Due to the well-known limitations of the PASAT, an alternative MSFC with the “Symbol Digit Modalities Test”(SDMT) instead of the PASAT, has also been proposed (MSFC-SDMT). The aim of this study is to investigate/compare the relationship between thalamic volume and disability measures (EDSS/MSFC/MSFC-SDMT) in pwMS.

Methods:: We enrolled 115 relapsing-remitting pwMS who underwent clinical (EDSS/MSFC/MSFC-SDMT) and 3T–MRI assessment. Thalamic volumes were calculated using FIRST tool of the FMRIB Software Library. Spearman correlations and linear regression models were applied to investigate the relationship between thalamic volumes and EDSS/MSFC/MSFC-SDMT or their subcomponents.

Results:: The MSFC-SDMT was the only significant independent predictor of the thalamic volume (Adj.R²=0.29;β=0.67;t=4.16;p<0.001). Replacing MSFC and MSFC-SDMT with their components (9HPT, T25FW, PASAT and SDMT) in the linear regression model, the SDMT was the only significant predictor of the thalamic volume (Adj.R²=0.28;β=0.47;t=3.95;p<0.001).

Conclusions:: Between most commonly used composite disability scales, MSFC-SDMT is the only independent predictor of thalamic volume. Moreover, this study further confirms that thalamic volume is more associated with cognitive than physical disability.
EFFICACY OF COMPUTER BASED COGNITIVE REHABILITATION IN MULTIPLE SCLEROSIS ACCORDING TO FREQUENCY OF TRAINING SESSIONS

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Background and Aims:: The cognitive impairments affect up to 75% from persons with multiple sclerosis (MS) and lead to significant disability in parallel with or independently of physical deficiency. Aim: to follow up the effect of computer based rehabilitation on cognition in MS patients according to the frequency of training sessions

Methods:: The cognitive rehabilitation was made through computer based module RilaCogniSoft which included training of the speed of information processing, visuo-spatial orientation, verbal learning and executive functions. Fifty subjects with definite MS at mean age 45.6±11.8 years (33 female, 17 male) were enrolled in the study. An individual rehabilitation program was composed with mean duration of the sessions 20 minutes. The patients were divided into 2 groups: 1) Group A, who made training sessions at every 5±3 days, 2) Group B who performed training at every 10±3 days. The period of cognitive rehabilitation lasted 3 months. The cognition was tested twice - before and after the rehabilitation period through a brief cognitive screening.

Results:: Persons from Group A showed significant improvement on cognition (p<0.05), while the persons from Group B increased their cognitive skills non substantially.

Conclusions:: Computer-based rehabilitation is recommended to be performed at least once a week in order to stimulate the cognitive brain reserve. The results from our study support the concept of inclusion of the cognitive rehabilitation to the overall therapeutic approach to persons suffering from MS. This research is supported by the Bulgarian National Science Fund under Grant Ref. No. KP-06-N22/1/2018 "Theoretical research and applications of InterCriteria Analysis".
PATIENT REPORTED OUTCOMES OF NEW BRAND-GENERIC PRODUCT OF TERIFLUNOMIDE (TEBAZIO®) IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS: PRELIMINARY ANALYSIS

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Background and Aims:: This study aimed to evaluate the patients’ treatment satisfaction after switching to a brand-generic Teriflunomide product (Tebazio®, 14 mg tablet) produced by Zistdaru Danesh biopharmaceutical company and report the tolerability and safety concerns during the period of the treatment.

Methods:: The study was conducted on 100 patients with confirmed diagnosis of MS with a EDSS 0 to 5.5 from Nov 2019 to Nov 2020. Study outcomes included patients’ satisfaction was measured by Treatment Satisfaction Questionnaire for Medication [Version 1.4] (TSQM) at baseline and week 24, disability status measured by EDSS score at baseline and week 24 after starting of Teriflunomide 14 mg, safety and tolerability evaluated over 6 months.

Results:: Patients reported significant improvements in treatment satisfaction scores of convenience and side effects domains of TSQM scores at week 24 following the switch to teriflunomide regardless of the reason for treating with teriflunomide (disease worsening: baseline, 66.53, Week 24, 68.97; convenience: baseline, 66.31, Week 24, 78.97; intolerance: baseline, 67.13, Week 24, 75.60; Global Satisfaction: baseline, 63 Week 24, 65.42; P < 0.001 in all comparisons). The most common adverse drug reactions were hair thinning (36%), dermatologic (17%), gastrointestinal (23%), liver function test dysfunction (11%) which all were mild to moderate and rarely caused treatment discontinuation.

Conclusions:: Patients reported significant satisfaction regarding TSQM scores after switching to Tebazio at week 24 which can be impressive to increase patient compliance. The 14 mg brand-generic Teriflunomide product was well tolerated in Iranian RRMS patients and no new alarming signal was detected during the study period.
ASSOCIATIONS BETWEEN MULTIPLE SCLEROSIS AND SKIN LESION: ABOUT FIVE CASES

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Background and Aims:: Vitiligo, Psoriasis and alopecia areata, a common chronic inflammatory disease, increases the risk of developing multiple sclerosis (MS), but evidence for this outcome is still unclear. This relation does not appear to be more common in patients with MS or their relatives. It may also be a rare side effect of treatment Related complication of MS.

Methods:: We conducted a retrospective study including one hundred patients followed for MS at the Neurology Department of the Main Military Hospital of Tunis (HMPIT) over a 16-year period from 2001 to 2020. The inclusion criterion was a definite diagnosis of MS meeting the criteria of Mc Donald 2017.

Results:: We collected 5 patients with MS and skin lesions. The mean age of onset was 34 years old. We reported an association of MS and psoriasis in three cases, vitiligo in one case and alopecia areata in one case. The mean duration between the diagnosis of skin lesion and the onset of MS was 17 years. Two patients developed psoriasis few months after initiation of Interferon-B therapy.

Conclusions:: Although there are some common genetic linkages in skin lesion and MS, psoriasis does not appear to be more common in patients with MS or their relatives. Further studies are warranted to establish the mechanisms underlying this relationship and its potential clinical consequences.
PSEUDOTUMORAL FORMS OF MULTIPLE SCLEROSIS: ABOUT 6 CASES

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Background and Aims:: Multiple sclerosis (MS) is the most common chronic disabling disease of the central nervous system (CNS) in young adults. It is characterized by the presence of multiple demyelinating inflammatory lesions disseminated in the CNS. Pseudotumoral lesions (PL) are rarely observed in patients with MS. The aim of this study is to describe characteristics of PL in patients with MS.

Methods:: We conducted a retrospective study including one hundred patients followed for MS at the Neurology Department of the Main Military Hospital of Tunis over a 16-year period from 2001 to 2020. The inclusion criterion was a definite diagnosis of MS meeting the criteria of Mc Donald 2017.

Results:: 6 patients (5 female, 1 male), with a mean age of 30 years, were identified. All of them suffered from a relapsing-remitting form of MS. 5 patients had symptomatic PL. one patient presented atypical clinical manifestations such as epileptic seizures. Full recovery was found in all our patients. After a mean follow-up of 43 months, recurrent PL episodes were not observed, the annualized relapse rate was 0.95 and the mean final EDSS score was 1.5. The majority of PL (5 patients) were supratentorial, coexisted with typical demyelinating plaques and showed the ring-like morphology and the ring pattern of contrast enhancement. One patient had an aspect of cystic mass.

Conclusions:: The PL of MS often represent a diagnostic problem. Our findings contribute to a better characterization of PL in patients with MS. However, larger studies are required to define this atypical entity more exactly.
FAMILIAL AND SPORADIC FORMS OF MS IN ALGERIA: ARE THERE DISTINCTIVE CLINICAL AND GENETIC FEATURES?

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Background and Aims:: Multiple sclerosis (MS) is a multifactorial disease implicating environmental factors and genetic susceptibility. The objective of this study is to describe the clinical and genetic characteristics of familial forms of MS and comparing them to sporadic forms.

Methods:: A cohort of 116 patients was studied, we identified two groups: 36 Familial MS (fMS) with history of first or second-degree relative affected by MS and 80 sporadic MS (sMS) with no family history of MS. All patients were genotyped for HLA class II alleles by PCR-SSP technique.

Results:: MS patients with familial form had an older age at onset compared to sMS group but statistically there is no significant difference (32.3 versus 30.8; p= 0.53). Relapsing form were predominant in the two groups (89% in group 1 and 95% in group 2; p= 0.41). Mean EDSS scores (3.1 versus 3.1), Median time to reach EDSS 4 (10 versus 9; p= 0.19) and MSSS scores (4.2 versus 4.3; p=0.91) were similar in the 2 groups. HLA-DRB1*1501 gene was present in 33% of fMS and in 36% of sMS (p=0.79). The severity of the disease was similar among most affected family members, especially in the siblings who share the same haplotype.

Conclusions:: As described in previous studies, we have not reported major differences between familial and sporadic forms of MS. Concordance in disease course and severity between family members has been found in most studies. HLA studies in siblings with MS reveal more common haplotypes than would be randomly expected.
ITALIAN TRANSLATION AND VALIDATION OF THE ABILHAND-26 AND ITS CORRELATION WITH UPPER LIMB OBJECTIVE AND SUBJECTIVE MEASURES IN MULTIPLE SCLEROSIS SUBJECTS

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Background and Aims:: Upper limb (UL) function affected in about 50% of people with MS (PwMS). In the last decade, Patient Reported Outcome Measures (PROM) are playing an important role in clinical trial and practice. ABILHAND-26 is a PROM that assess self-perceived manual ability defined as the capacity to manage daily activities using the upper limbs. The aim of the study is to translate the ABILHAND-26 into Italian, to explore its psychometric properties examining the associations with demographics, clinical variables, 9-Hole Peg Test (9-HPT) and Manual Ability Measures-36 (MAM-36).

Methods:: Subjects were recruited in five Italian neurological centers. They were evaluated through ABILHAND-26, 9-HPT and MAM-36. Confirmatory factor analysis and Rasch analysis were adopted to investigate the psychometric properties of the ABILHAND-26.

Results:: Two hundred and forty-five patients were recruited. Rasch analyses showed adequate functioning and supported the unidimensionality of the scale. ABILHAND-26 negative correlations with age and disease duration, moderate negative correlation with EDSS and the 9-HPT scores for both arms and strong positive associations (ρ ≥ .84) with the MAM-36. Difference in ABILHAND scores only emerged when comparing patients with higher disability (EDSS ≥ 6) with both the other groups (p < .01)

Conclusions:: The Italian version of the ABILHAND-26 in now available. It shows adequate reliability of the score, good convergent validity, moderate criterion validity and strong convergent validity. ABILHAND-26 is a valid assessment for self-perceived ability to perform manual activity, especially for PwMS with moderate-to-high level of disability.
CORRELATION BETWEEN MANUAL ABILITY MEASURE-36 AND THREE UPPER LIMB OBJECTIVE MEASURES IN PEOPLE WITH MULTIPLE SCLEROSIS

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Background and Aims:: Upper limb (UL) function is often affected in people with Multiple Sclerosis (PwMS) and it is usually assessed through objective measures: Nine Hole Peg Test (9-HPT), Box and Block Test (BBT), Hand Grip Strength (HGS). However, subjective self-perceived manual ability should be assessed through Manual Ability Measure-36 (MAM-36). The study aims to evaluate correlations between 9-HPT, BBT, HGS and MAM-36 to understand impact of UL dysfunction in MS.

Methods:: The multicenter study included 5 Italian neurological centers. Subjects were assessed through 9-HPT, BBT, HGS, MAM-36 and Spearman correlations were computed in the whole sample, by EDSS and disease course.

Results:: 199 PwMS were included: 128 females, mean age 50.69 (13.05) years, 119 relapsing-remitting, 31 primary and 49 secondary progressive MS, mean disease duration 13.97 (10.41) years, mean EDSS 4.58 (1.97).

Results in the whole group showed 9-HPT had small-to-moderate significant negative correlations with the MAM-36, while BBT and HGS showed small-to-moderate positive associations with the MAM-36. As regards the correlation computed in the different EDSS subgroups: 9HPT: significant associations between the 9HPT and MAM-36 scores in severe disability group (EDSS ≥ 6).

HGS: moderate positive associations with MAM-36 in mild and moderate groups.
BBT: small-to-moderate positive correlation with MAM-36 in severe disability group.

Conclusions:: Correlations between objective measures and MAM-36 were overall small-to-moderate, meaning that subjective perception is not covered by objective measures. In particular, 9HPT and BBT showed significant association with MAM-36 in severe disability group with HGS in mild and moderate disability groups.
THE TRAJECTORY OF FUNCTIONAL DISORDERS IN EARLY DIAGNOSED PEOPLE WITH MULTIPLE SCLEROSIS: 1-YEAR FOLLOW-UP STUDY

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Background and Aims:: There are limited research aimed at understanding the multidimensional trajectory of functional disorders overtime in early diagnosed People with Multiple Sclerosis (PwMS). The study aims to investigate progression of disability, walking endurance, fatigue, manual dexterity and cognition in a cohort of PwMS in early disease stage.

Methods:: Eighty-two subjects were assessed at baseline (BL) and 46 PwMS (age:39.5±10.6 years, Expanded Disability Status Scale (EDSS)≤2.5, disease duration≤5 years) were assessed and followed prospectively over 1-year period (FU). Data collected: EDSS, Six-Minutes Walking Test (6MWT), Fatigue Severity Scale (FSS), Multiple Sclerosis Walking Scale-12 (MSWS-12), Nine Hole Peg Test (NHPT), Symbol Digit Modality Test (SDMT).

Results:: Percentages of abnormal scores:6MWT: BL=28%, FU=32%; FSS: BL=23%, FU=17%; MSWS-12: BL=51%, FU=58%; NHPT: BL=27%, FU=27%; SDMT: BL=10%, FU=2 %. Changes at FU: 6(13%) out of 46 subjects deteriorated at the EDSS using a cut-off of 0.5 points increment. A higher percentage was observed for 6MWT (n=8, 18%,cut-off≤55m), followed by MSWS-12 (n=7, 15%,cut-off≤4 points), FSS (n=6, 15%,cut-off≤2 points), SDMT(n=4, 9%,cut-off≤10%), NHPT(n=2, 4%,cut-off≤20%). Weak correlations (from-.01 to .25) between changes at EDSS and changes in functional scales were observed. Correlations among changes in functional scales ranged between .04 to .55.

Conclusions:: Walking impairments measured by 6MWT and MSWS-12 progressed faster than manual dexterity and cognitive disorders. Changes at EDSS did not correlate with changes in functional tools suggesting that EDSS is not sensitive enough to detect deterioration in functional disorders. Walking impairments should be assessed in this population using specific tools to early detect functional disorders and set up tailored preventive interventions.
MILIARY DISTRIBUTION OF MRI RING-ENHANCING BRAIN LESIONS: AN ATYPICAL PRESENTATION OF MULTIPLE SCLEROSIS

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¹University of Ferrara, Sant’Anna Hospital, Clinical Neurology, Ferrara, Italy, · Ferrara Hospital, Neurology, Ferrara, Italy

Background and Aims:: Ring-enhancing lesions are one of the most frequently encountered abnormalities on neuroimaging and can be expression of infectious, neoplastic, vascular or inflammatory disease. In particular, they are currently considered a possible radiological pattern of Multiple Sclerosis (MS) [1]. We report a case of Multiple Sclerosis with atypical ring-enhancing lesions: clinicians should be aware of the possible unusual radiological presentation of this very common inflammatory disease.

Methods:: A 27-year-old woman presented to Emergency Department with left brachio-crural weakness. MRI showed diffuse, “miliary”, T2-FLAIR hyperintense, T1-hypointense, ring-enhancing white matter lesions, attempting supratentorial brain regions, cerebellum and spinal cord. Cerebral Spinal Fluid (CSF) profile revealed moderate lympho-plasmacellular pleiocytosis. Patient started intravenous Desamethasone, with good response.
Results: Autoimmune, neoplastic and infectious diseases were ruled out. Anti aquaporin-4 and anti-MOG antibodies resulted negative. We finally found multiple CSF IgG clonal bands, so the diagnosis of definite MS was posed. Patient underwent two more disease relapses responsive to corticosteroids and finally started Ocrelizumab, showing radiological and clinical improvement (actual moderate residual paraparesis).

Conclusions: Ring-enhancing lesions are considered a possible MS radiological pattern, usually appearing as single or a few, open ring-enhancing lesions [2]. This case was unusual because brain MRI showed a great amount of very little lesions (< 12 mm diameter) with closed ring-enhancement, mimicking infectious or neoplastic disease. Negativity of all investigations, good response to steroidal therapy and CSF finding of multiple IgG clonal bands supported diagnosis of MS, sometimes very challenging for
A GENE-SET ANALYSIS SUGGESTS THE POSSIBLE INVOLVEMENT OF IRON HOMEOSTASIS IN NEURODEGENERATION IN PROGRESSIVE MULTIPLE SCLEROSIS

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1IRCCS San Raffaele Scientific Institute, Neurology Unit, Neurorehabilitation Unit And Neurophysiology Service, Milan, Italy, 2IRCCS San Raffaele Scientific Institute, Laboratory Of Human Genetics Of Neurological Disorders, Milan, Italy, 3IRCCS San Raffaele Scientific Institute, Neuroimaging Research Unit, Division Of Neuroscience, Milan, Italy

Background and Aims:: Advanced neuroimaging has revealed that slowly expanding lesions with a paramagnetic iron rim are the most common lesion type in progressive multiple sclerosis (pMS) and correlate with disability. Iron accumulation in the activated microglia and macrophages at the edge of these lesions is governed by inflammatory pathways and may contribute to the pathogenesis of pMS. We investigated whether genetic variants in genes involved in iron metabolism may have an impact on pMS.

Methods:: After selecting a set of 312 genes deemed relevant for iron homeostasis from KEGG and Gene Ontology sources, we performed an association analysis to test the impact of single-nucleotide polymorphisms (SNPs) in these genes on the development of pMS, comparing relapsing-remitting (RR) MS patients who did not experience disease progression after 20-years from disease onset versus primary progressive (PP) MS patients.

Results:: We included 830 patients (RR:243, PP:508) and 4,594 SNPs mapping to the selected genes, retrieved from available whole-genome data. One SNP, rs16902359, passed the threshold for a significant association with the progressive course (p=2.19e-05; OR=0.48). Rs16902359 lies within CASC11 (Cancer Susceptibility-11), a long non-coding RNA gene, implicated as transcriptional activator in glial and neural tumorigenesis. In addition, rs16902359 has an expression- and methylation-Quantitative-Trait-Loci effect on the adjacent MYC gene, a key player in iron homeostasis, apoptosis and neurodegeneration, involved in the pathogenesis of other neurodegenerative diseases.

Conclusions:: CASC11 and MYC genes, that are involved in iron metabolism and neurodegeneration, appear to have a role in the development of pMS. These results need to be confirmed in larger and independent cohorts.
Background and Aims: NMOSD is an immune-mediated disorder which is characterized by relapsing episodes of optic neuritis and myelitis. Brain stem related symptoms such as intractable vomiting are not usually considered as the initial presentation and misdiagnosis has been frequently observed. Almost 4% of NMOSD cases are pediatric. Early differentiation of NMOSD from other childhood disorders including ADEM, MS, infections and mass lesions is critical.

Methods: An 11 years old girl presented with intractable vomiting and received several types of gastrointestinal treatments during one month. After that diplopia occurred and also she suffered vertigo. In this stage Brain MRI showed isolated edematous intramedullary lesion with heterogeneous enhancement. Patient received corticosteroid therapy with diagnosis of brain stem mass and the symptoms improved. She was candidate for biopsy to decide for radiation or chemotherapy but her parents didn’t accept. After three months she developed central facial nerve palsy, the brain MRI showed the same lesion. Anti AQP4 ab was positive, so the appropriate treatment started with final diagnosis of NMOSD.

Results: Only about 30% of patients presents with brainstem involvement. It is difficult to diagnosis of NMOSD with presentation of acute brainstem or cerebral or diencephalic syndromes for physicians who are not familiar with its clinical features and diagnostic criteria. Involvement of the area postrema can lead to the initial presentation of sometimes intractable nausea and vomiting with associated intramedullary lesions on MRI in 16% to 43% of patients.

Conclusions: NMOSD should be considered in differential diagnosis of isolated brain stem lesions to avoid from invasive surgical interventions. Early diagnosis is critical for proper treatment.
TREATMENT WITH NATALIZUMAB DURING THE COVID-19 PANDEMIC IN MULTIPLE SCLEROSIS PATIENTS

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University Hospital Clínico San Carlos, Neurology. Multiple Sclerosis Center, Madrid, Spain

Background and Aims:: Multiple sclerosis patients treated with highly active treatments (natalizumab, ocrelizumab) have an increased risk of infections. Natalizumab discontinuation can produce a rebound effect, consisting of severe disease reactivation. We aim to study the management and safety of MS patients on natalizumab during the Covid-19 pandemic.

Methods:: Prospective study of MS patients on natalizumab during COVID-19 pandemic. We evaluate demographic features, time on natalizumab, dose interval, and COVID-19 symptoms. RT-PCR COVID-19 tests from nasopharyngeal sample were performed before every natalizumab infusion.

Results:: We analyzed 69 patients: 71% women, mean age: 43. The mean treatment duration was 68 months (range: 2-141). In 32% of patients natalizumab was changed from every 4 weeks to every 6w to decrease visits to the hospital. From March to April 2020, 5 patients had COVID19 (tables 1-2). On May 2020 we started Covid-19 screening before natalizumab infusion. From May 2020 to March 2021, 553 nasal swab PCR COVID-test were performed. Fourteen patients showed a positive result and natalizumab was stopped; test was repeated 1-2 weeks later with a negative result and natalizumab was restarted. In summary: 28% of patients had COVID19, 90% asymptomatic or mild symptoms and only 2 patients required specific treatment (tables 1-2). There were no statistically significant differences in the age (p0.158), dose interval (p0.962) or treatment duration (p0.298) between patients with COVID19 and non-COVID19.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Natalizumab dosage</th>
<th>Time on natalizumab</th>
<th>Symptoms</th>
<th>PCR</th>
<th>Time</th>
</tr>
</thead>
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<tr>
<td>Woman</td>
<td>44</td>
<td>6w</td>
<td>12m</td>
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<td>First wave</td>
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<tr>
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</tr>
<tr>
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<td>130m</td>
<td>Yes</td>
<td>Not performed</td>
<td>First wave</td>
</tr>
<tr>
<td>Woman</td>
<td>35</td>
<td>4w</td>
<td>79m</td>
<td>Yes</td>
<td>Not performed</td>
<td>First wave</td>
</tr>
<tr>
<td>Woman</td>
<td>43</td>
<td>6w</td>
<td>79m</td>
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<td>Second wave</td>
</tr>
<tr>
<td>Man</td>
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<td>6w</td>
<td>139m</td>
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</tr>
<tr>
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<td>Second wave</td>
</tr>
<tr>
<td>Woman</td>
<td>49</td>
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<tr>
<td>Woman</td>
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<td>48m</td>
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<td>Second wave</td>
</tr>
<tr>
<td>Woman</td>
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<tr>
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</tr>
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<td>58m</td>
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</tr>
<tr>
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<td>64m</td>
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</tr>
<tr>
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<td>6w</td>
<td>44m</td>
<td>Yes</td>
<td>Positive</td>
<td>Second wave</td>
</tr>
<tr>
<td>Man</td>
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<td>6w</td>
<td>19m</td>
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<td>Positive</td>
<td>Second wave</td>
</tr>
<tr>
<td>Man</td>
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<td>72m</td>
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<td>Positive</td>
<td>Second wave</td>
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<tr>
<td>Woman</td>
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<td>6w</td>
<td>105m</td>
<td>Yes</td>
<td>Positive</td>
<td>Second wave</td>
</tr>
<tr>
<td>Woman</td>
<td>33</td>
<td>6w</td>
<td>66m</td>
<td>Yes</td>
<td>Positive</td>
<td>Second wave</td>
</tr>
</tbody>
</table>
**Conclusions:** Natalizumab treatment seems to be safe in MS patient during COVID-19 pandemic. Most patients were asymptomatic and no patient required mechanical ventilation.
Background and Aims:: Myelin oligodendrocyte glycoprotein associated disease (MOGAD) features may overlap with relapsing-remitting multiple sclerosis (RRMS). Little is known about brain atrophy occurrence in MOGAD. This study compares rates of brain volume change over time in MOGAD and RRMS patients.

Methods:: 18 adult MOGAD patients (10 females) were selected from a multicentric observational study in which they had been previously enrolled. 33 RRMS patients (17 females), matched for age and sex to the MOGAD cases were recruited in the Verona MS centre. Availability of two brain MRI scans performed in an interval of 6-30 months and a clinical follow-up ≥6 months were mandatory for each patient. The same MRI protocol and scanner at both timepoints was used for each patient. Annualised percentage brain volume change (PBVC/y) between the two MRI timepoints, baseline global brain, grey and white matter (WM), and regional volumes were compared between groups.

Results:: Mean PBVC/y was lower in MOGAD than in RRMS in a subgroup of patients aged <60 years and with a disease duration ≤10 years (p=0.046). Overall, mean global brain volume was higher in MOGAD (p=0.021) as well as mean WM volume (p<0.001); mean putaminal volume was lower in MOGAD (p=0.003). Median T2-lesion volume at timepoint 1 was lower in MOGAD (p<0.001); T2-lesion volume increased between the 2 MRI timepoints in RRMS (p<0.001) but not in MOGAD (p=0.11).

Conclusions:: MOGAD displays less global brain and WM atrophy than RRMS, as well as less brain volume loss and lesion load over time, suggesting different neuropathogenic mechanisms underlining the two diseases.
ITALIAN MULTICENTER OBSERVATIONAL STUDY ON REAL-LIFE EXPERIENCE WITH ALEMTUZUMAB IN NAÏVE PATIENTS WITH AGGRESSIVE MULTIPLE SCLEROSIS

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Background and Aims:: Alemtuzumab(ALEM) is an anti-CD52 monoclonal antibody approved for the treatment of active Multiple Sclerosis(MS) which showed high efficacy also in the subgroup of highly-active patients. We aimed to evaluate efficacy/safety profile of ALEM-treatment in a population of aggressive MS naïve-patients.

Methods:: We conducted a multicenter prospective observational study in a cohort of aggressive naïve-patients treated with ALEM. Clinical and neuroradiological parameters were collected from clinical records in 29 Italian MS Centers from October 2015 to February 2021.

Results::
<table>
<thead>
<tr>
<th>Table 1. Basal Characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients included</td>
<td>133</td>
</tr>
<tr>
<td>Age at treatment, mean ± SD</td>
<td>31.4 ± 8.9</td>
</tr>
<tr>
<td>Sex: Females - Males, n(%)</td>
<td>F: 80 (60.2) – M: 53 (39.8)</td>
</tr>
<tr>
<td>Time to treatment from disease onset (months), median (IQR)</td>
<td>8 (4 – 27)</td>
</tr>
<tr>
<td>Follow-up in months, mean ± SD</td>
<td>34.2 (12.1)</td>
</tr>
<tr>
<td>Baseline EDSS, median (IQ range)</td>
<td>3.0 (2.0 – 3.5)</td>
</tr>
<tr>
<td>ARR previous year, mean ± SD</td>
<td>1.8 ± 0.9</td>
</tr>
<tr>
<td>Number of brain T2-hyperintense lesions at MRI baseline, mean ± SD</td>
<td>29.8 ± 20.8</td>
</tr>
<tr>
<td>Number of brain Gd+ lesions at MRI baseline, mean ± SD</td>
<td>3.4 ± 5.1</td>
</tr>
<tr>
<td>Number of spinal cord T2/STIR-hyperintense lesions at MRI baseline, mean ± SD</td>
<td>5.0 ± 3.0</td>
</tr>
<tr>
<td>Number of spinal cord Gd+ lesions at MRI baseline, mean ± SD</td>
<td>0.9 ± 1.5</td>
</tr>
</tbody>
</table>
33 naïve-patients were included. Basal characteristics are shown in Table1. Efficacy data were analyzed after the end of the complete therapeutic cycle (2 ALEM-courses) because presence of disease activity between the two courses is not indicative of a therapeutic failure. Follow-up data at 24 and 36 months were available for 99/133 and 61/133 subjects, respectively. NEDA-3 at 24 and 36 months was reached by 89.2% and 69.4% of patients, respectively. At 24 and 36 months mean ARR were 0.06 and 0.1; median EDSS were 2.0 and 1.5, respectively. At the same time-points, mean increase in T2 lesions was
0.2 and 0.48 respectively. 5.3% of patients needed a third cycle of therapy. Overall 74.4% of patients reported adverse events (Table2).

Conclusions:: These results highlight that aggressive naïve-patients are an ideal candidate for immune system resetting, likely due to young age, short disease duration and low disability. Furthermore, absence of previous immunomodulating/immunosuppressant drugs altering the immune system play a key role in determining effectiveness of this powerful drug. Longer FU is needed to confirm our data.
EFFECTS OF INTERMITTENT APPLICATION OF TRANSCRANIAL DIRECT CURRENT STIMULATION COMBINED WITH STATIONARY BICYCLE IN IMPROVING GAIT IN MULTIPLE SCLEROSIS

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Background and Aims:: The exercise therapy program has proved to be safe and well-tolerated for multiple sclerosis (MS) patients. Recently, physical therapy combined with transcranial direct current stimulation (tDCS) has been shown to reinforce the therapeutic effects in neurorehabilitation. The present study aimed to evaluate the therapeutic efficacy of tDCS along with a stationary bike in improving gait among MS patients.

Methods:: This randomized double-blinded controlled trial (RCT) was conducted on 50 eligible individuals with MS. A total of 39 participants completed the study. 21 in the active and 18 in the sham group. The subjects were randomly assigned to receive exercise along with anodal tDCS, or exercise alone utilizing stationary bike plus a sham-tDCS protocol. The study goal was to determine and compare walking performance tests, [2-minute walk test (2MWT), 5-Meter Walk Test (5MWT), and Timed Up and Go test (TUG)]. Manual muscle test (MMT), fatigue severity scale (FSS), and multiple sclerosis quality of life-54 (MSQOL-54) questionnaires.

Results:: In terms of the observed changes in 2MWT and 5MWT, all the post-treatment values were better for the interventional group than the exercise-alone group. After intervention and one month later, the mean TUG value statistically decreased significantly in the combinational-treatment group (P=0.002) than the control group. On the other hand, there was no preference between the two groups in terms of FSS score, MSQOL-54, and MMT improvement.

Conclusions:: Intermittent application of anodal tDCS combined with cycling can lead to better results in walking speed of MS subjects comparing to exercise alone.
CONTINUOUS USE OF INTERFERON BETA-1B IN MULTIPLE SCLEROSIS PATIENTS WITH CANCER

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Background and Aims:: There is limited available data regarding the use of disease modifying therapies (DMT) in multiple sclerosis (MS) patients with newly developed malignancies and there are currently no accepted guidelines for the management of such patients. We are presenting two cases of continuous use of DMTs in patients with MS and cancer.

Methods:: From our clinic’s MS database, we retroactively selected the few cases in which the use of DMTs was not interrupted in MS patients who developed cancer.

Results:: A 31 years old patient diagnosed with relapsing remitting multiple sclerosis (RRMS) (EDSS=1.5) and treated with Interferon beta 1b, developed desmoplastic nodular medulloblastoma 7 years later. The DMT was not interrupted during or after radiotherapy and the surgical removal of the tumor. Currently, 14 years after the MS diagnosis, the patient has an EDSS score of 6 and is cancer free on multiple MRI scans. Another 45 years old patient was treated with Interferon beta 1b for 5 years for RRMS (EDSS=1.5) prior to her developing cervical cancer. The DMT was not interrupted during or after radiotherapy and removal of the tumor. Now, 15 years after the cancer diagnosis, the patient has EDSS score of 4.5 and is cancer free.

Conclusions:: Although the current guidelines make no recommendations for the use of DMTs on active cancer patients, it was our patients’ wish to continue the treatment. For 15 and respectively 7 years after the cancer diagnosis, the patients continue using Interferon beta 1b, experiencing no cancer relapses.
FASUDIL PROMOTED REMYELINATION IN CPZ-INDUCED MICE BY REGULATING THE FUNCTION OF ASTROCYTES

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Background and Aims:: Fasudil, a ROCK inhibitor, has been exhibited its advantageous roles in demyelinating diseases. Previous researches have shown that Fasudil performs multiple functions including immunomodulation, neurotrophy, neuro-axonal regeneration and myelin protection. Our aim was to observe the myelin protection and potential mechanisms of Fasudil in Cuprizone (CPZ)-induced mice model.

Methods:: Male C57BL/6 mice were divided into three groups: Control group was fed with standard diet, while CPZ demyelinating model was fed with 0.2% CPZ diet for 6 weeks, which were divided into model and Fasudil treatment group. Fasudil treatment group received intraperitoneal injection (i.p.) of Fasudil (40mg/kg/d) in the last two weeks, while Control and model mice were injected with saline (i.p.).

Results:: Fasudil improved anxiety/depression-like behaviors. Immunofluorescence staining showed that Fasudil increased the phagocytosis of myelin debris by GFAP+ astrocytes and the number of BDNF+GFAP+ astrocytes in the corpus callosum of CPZ mice. Fasudil also enhanced the expression of Sox2 by GFAP+ astrocytes and induced astrocytes to express a marker of OPCs (NG2), implying that Fasudil may promote the transformation of astrocytes into OPCs.

Conclusions:: Fasudil may increase astrocytes to phagocytize myelin debris and induce astrocytes to express neurotrophic BDNF as well as translation factor Sox2 and promote astrocytes to differentiate into myelinogenic cells, therefore, improving behaviors and promoting the remyelination of CPZ mice. (NNSF of China 81473577, Open Projects of The Key Laboratory of The Ministry of Education 2019004 and Chinese Academy of Sciences 2020-MDB-KF-09, China Postdoctoral Science Foundation 2020M680912, Ma and Xiao are corresponding authors)
REAL WORLD EXPERIENCE WITH CLADRIBINE AT S.ANDREA HOSPITAL OF ROME

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Background and Aims:: Among drugs used for Multiple Sclerosis (MS), Cladribine (Mavenclad) is the most recent commercially available in Italy. Here, we report the real world experience from patients treated with Cladribine in our MS Center.

Methods:: Clinical data included Expanded Disability Status Scale (EDSS) scores and relapses. Confirmed disability improvement (CDI) and confirmed disability worsening (CDW) was defined by a 1 point increase or decrease in the EDSS score respectively. MRI findings were also recorded.

Results:: We collected data from 60 patients (11 males; 49 females). Fifty-six patients had a relapsing remitting course (RRMS), 4 patients had a secondary progressive phenotype (SPMS). Mean age at baseline was 35,40 +/- 8,79. Mean and median EDSS at baseline was 2,8 and 2,5 (range 1-5.5) respectively. Prior to Cladribine, 29 patients received 2 or more disease modifying treatments (DMTs), 13 patients had 1 DMT and 18 patients were naïve. The mean follow-up was 16 months +/-9.38. CDI was found in 6 patients and CDW in 2 patients. Four patients had relapses. Follow-up MRIs was available up to now in 34 patients, 10 of them show at least one new MRI lesion. No adverse events were reported except for 1 case of recurrent cystitis and 1 of lymphopenia grade 3. Only one patient was shifted to another DMT for lack of efficacy.

Conclusions:: These data provide information on routine use of Cladribine while the most existing knowledge about the use of Cladribine comes from phase 3 clinical trials.
CSF CXCL13 AND CHITINASE 3-LIKE-1 CONCENTRATIONS PREDICT DISEASE COURSE IN RELAPSING MULTIPLE SCLEROSIS

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Background and Aims:: Several biomarkers from MS patients' biological fluid have been evaluated to support a more precise diagnosis, to predict disease course, and to evaluate treatment response. We investigated the diagnostic and prognostic value of CSF concentration of target biomarkers in both relapsing (RMS=107) and progressive (PMS=18) MS patients and in other inflammatory (OIND=10) and non-inflammatory (ONIND=15) neurological disorders.

Methods:: We evaluated the CSF concentration of APRIL, BAFF, CHI3L1, CCL-2, CXCL-8, CXCL-10, CXCL-12, CXCL-13 through a Luminex Assay. MS patients were prospectively evaluated, and clinical and radiological activity were recorded.

Results:: CHI3L1 and CXCL13 CSF levels were significantly higher in both MS groups compared to both control groups while CCL2, BAFF, and APRIL concentrations were lower in RMS patients compared to PMS and OIND. Higher concentrations of CHI3L1, CXCL10, CXCL12, and CXCL13 were registered in patients with single demyelinating event who convert to clinically defined MS. RMS patients in the CXCL13 and CHI3L1 high concentration group have a significantly higher risk of relapse (HR 12.61 and 4.57,p<0.001), MRI activity (HR 7.04 and 2.46,p<0.001), and of any evidence of disease activity (HR 12.13 and 2.90,p<0.001) during follow-up.

Conclusions:: CSF CXCL13 e CHI3L1 levels represent very good prognostic biomarkers in RMS patients and therefore can guide the treatment choice. Higher CSF concentrations of neuro-inflammatory biomarkers were associated with a higher risk of conversion to CDMS in patients with a first clinical demyelinating event. Differential CSF BAFF and APRIL levels between RMS and PMS suggest a different modulation of B-cells pathways in the different phases of the disease.
PATTERNS OF USE AND EFFECTIVENESS OF ANALGESICS AND CANNABINOIDS FOR PAIN RELIEF AMONG IRISH PATIENTS WITH MULTIPLE SCLEROSIS.

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Background and Aims:: Pain is an often-reported symptom in Multiple Sclerosis (MS); however, pain management is often described as being inadequate. Emerging evidence suggests that cannabinoids may be effective in the treatment of MS related pain. This research aimed to determine the prevalence and patterns of use of medications and cannabinoids for pain relief in a sample of Irish patients with MS.

Methods:: This was a cross-sectional survey. 101 individuals attending neurology outpatient appointments at Cork University Hospital completed questionnaires measuring demographics, severity of disability, nociceptive pain, neuropathic pain, use of medications, use of cannabinoids and degree of depression.

Results:: 59% (95% CI 48-67.7%) of patients had experienced MS related pain, while 26% (95% CI 17–34%) had experienced neuropathic pain. Prescription medication had been used by 73% (95% CI 62-84%) of participants with pain. 30% (95% CI 18–42%) of patients experiencing pain had used cannabinoids. Patients who had used cannabinoids compared to non-users were more likely to experience neuropathic pain, be of a younger age and to use cannabinoids recreationally (p< 0.05). In addition, the type of cannabinoids participants used appeared to influence how effectively they rated it as a pain reliever; with cannabis/hash being rated as more effective than CBD oil or a Sativex spray (p< 0.05).

Conclusions:: Pain is a significant problem for patients with MS which the current therapeutic options have failed to control. A substantial number of patients used cannabinoids to manage their pain, however further research into the efficacy and long-term side effects of this substance is necessary.
PREVALENCE OF SARS-COV-2 ANTIBODIES IN MULTIPLE SCLEROSIS: THE HIDDEN PART OF THE ICEBERG

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Background and Aims:: We compared the prevalence of SARS-CoV-2 IgG/IgM in multiple sclerosis (MS), low-risk, and high-risk populations and explored possible clinical correlates.

Methods:: In this cross-sectional study, we recruited MS patients, low-risk (university sta from non-clinical departments), and high-risk individuals (healthcare sta from COVID-19 wards) from 11 May to 15 June 2020. We used lateral flow immunoassay to detect SARS-CoV-2 IgG and IgM. We used t-test, Fisher’s exact test, chi square test, or McNemar’s test, as appropriate, to evaluate between-group differences.

Results:: We recruited 310 MS patients (42.3 ± 12.4 years; females 67.1%), 862 low-risk individuals (42.9 ± 13.3 years; females 47.8%), and 235 high-risk individuals (39.4 ± 10.9 years; females 54.5%). The prevalence of SARS-CoV-2 IgG/IgM in MS patients (n = 9, 2.9%) was significantly lower than in the high-risk population (n = 25, 10.6%) (p < 0.001), and similar to the low-risk population (n = 11, 1.3%) (p = 0.057); these results were also confirmed after random matching by age and sex (1:1:1). No significant differences were found in demographic, clinical, treatment, and laboratory features. Among MS patients positive to SARS-CoV-2 IgG/IgM (n = 9), only two patients retrospectively reported mild and short-lasting COVID-19 symptoms.

Conclusions:: MS patients have similar risk of SARS-CoV-2 infection to the general population, and can be asymptomatic from COVID-19, also if using treatments with systemic immunosuppression.
THE “NO EVIDENCE OF DISEASE ACTIVITY” (NEDA) CONCEPT IN MS: IMPACT OF SPINAL CORD MRI

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Background and Aims:: Measures to define treatment response, such as no evidence of disease activity (NEDA), are routinely used in multiple sclerosis (MS) clinical practice. Although spinal cord involvement in MS is frequent and strongly correlated with future disability accrual, its magnetic resonance imaging (MRI) monitoring, in the absence of spinal cord symptoms, is not routinely performed. This study aimed to assess the impact of spinal cord imaging and specifically, the impact of missing asymptomatic spinal cord lesions, in the definition of NEDA status in a cohort of MS patients treated with disease-modifying therapies (DMTs).

Methods:: We selected for the study 115 patients treated with first line DMTs undergoing clinical and MRI routine monitoring, for whom MRI was extended at least to the study of the cervical spinal cord. We retrospectively analyzed for the presence or absence of NEDA in the whole cohort, either considering or not spinal cord monitoring data for the definition of MRI disease activity.

Results:: When considering only clinical and brain MRI measures, 97 out of 115 patients (84.3%) satisfied the criteria for NEDA. In this same cohort, the percentage of patients who showed NEDA decreased to 76.5% (88 out of 115 subjects) when considering also spinal cord imaging data.

Conclusions:: These findings suggest that, in routine clinical practice, spinal cord MRI monitoring in patients under first line DMTs, leads to a slight but significant change in the proportion of subjects classified as clinically and radiologically stable according to the definition of NEDA.
MR NEUROGRAPHY UNRAVELS MYSTERY OF COLD ABSCESS

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Background and Aims:: This is a case report of a 24-year-old migrant laborer who came to neurology outpatient clinic with weakness of hypothenar and lumbrical muscles of left hand associated with painless swelling above the medial epicondyle.

Methods:: Complete neurological examination including assessment of peripheral neuropathy was done. Nerve electrophysiologic study and ultrasonography along with MR neurography was performed.

Results:: On examination there was palpable firm swelling in the medial lower part of left arm with hypopigmented patch over his left face. Neurological examination revealed only left ulnar neuropathy which was confirmed on electrophysiological studies. Left ulnar nerve ultrasound revealed round hypoechoic area above the thickened ulnar nerve and fusiform thickening extending up to the axilla. MR neurography of bilateral upper limb revealed hyperintense thickened left ulnar nerve through out its course (8.8 mm) with loss of fascicular architecture, proximally extending to involve inferior trunk of brachial plexus and medial cord while distal thickening till cubital tunnel. Forearm part of ulnar nerve was normal. There was associated hyperintense collection 2.2 X 1.4 cm communicating with the ulnar nerve 6 cm proximal to the elbow joint. Skin smear and aspiration of the collection confirmed the diagnosis of tubercular leprosy.

Conclusions:: This is the first case report highlighting the MR imaging characteristics of thickened ulnar nerve with extension till brachial plexus and communicating abscess in a patient of tubercular leprosy. Another unique finding in our patient was isolated involvement of single nerve with development of nerve abscess in the absence of any prior treatment for leprosy.
BEYOND THE DISABILITY, WHAT IS THE QUALITY OF LIFE IN ALGERIAN PATIENTS WITH MULTIPLE SCLEROSIS?

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Background and Aims:: Multiple sclerosis (MS) is the most common chronic progressive and disabling neurological disease of the CNS. It has many impacts on social, family and professional life. These repercussions have often been discussed in terms of quality of life. The purpose of this study is to assess quality of life, fatigue, and depression in MS patients.

Methods:: The clinical types, quality of life (Multiple Sclerosis Quality of Life-59), two depression scales (MADRS and HDRS) and fatigue levels (Fatigue Severity Scale - FSS) were carried out in 66 patients.

Results:: The mean age of the patients was 38.4 ± 2.4 years, and the mean disease duration was 8.1 ± 6.2 years. The mean EDSS was 3.66 ± 2.18. 93.9% of patients had relapsing-remitting MS. All dimensions of quality of life seemed to be impaired, 33.3% of patients had limitations related to physical activity, 34.8% of patients had memory problems, the fatigue was found in 68.2% of cases. Sexual disorders were present in 56.3% of men, and in 40% of women. Mood disorders and depression in 10% of cases

Conclusions:: Quality of life measures are bound to develop, with the aim of improving the quality of care. For the practitioner, the results of a quality of life questionnaire can be a valuable aid in detecting important problems and facilitating communication with the patient. Living as normally as possible is one of the challenges raised by multiple sclerosis.
BALO’S CONCENTRIC SCLEROSIS MIMICKING AN INTRACRANIAL SPACE OCCUPYING LESION IN A NIGERIAN ADULT MALE: A CASE REPORT

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Background and Aims:: Baló’s concentric sclerosis (BCS) is a rare demyelinating disease often classified as a variant of multiple sclerosis. Typically, brain MRI shows concentric lamellae of demyelination alternating with normal zones of myelin preservation. Given its presentation with mass effect, it may be mistaken for other intracranial space occupying lesions (ICSOL), especially in our sub-region where neuroimaging facilities are scarce or not easily affordable. To the best of the authors’ knowledge, this is the first reported case of BCS in sub-Saharan Africa. Aims: We report the management and early outcome of a young Nigerian man managed for BCS in our hospital.

Methods:: Case report

Results:: The patient presented with behavioral changes, focal seizures, cranial neuropathy, long tract signs and cerebellar dysfunction causing severe disability and functional impairment with modified Rankin score (mRS) of 4. Brain MRI showed multiple heterogeneous lesions in the right cerebral hemisphere, brainstem and cerebellum with features in keeping with BCS. Cerebrospinal fluid oligoclonal bands were negative and C-reactive protein was normal. He received high doses of intravenous steroid therapy and was subsequently maintained on oral steroids and immunosuppressive therapy. He made gradual neurological improvement and significant symptom resolution and was able to return to work after about a year (mRS 1). He has been followed up for 18 months without relapse.

Conclusions:: Although BCS is a rare entity, it should be considered a differential diagnosis of ICSOL in our sub-region and high index of suspicion and prompt neuroimaging is required for early diagnosis.
TRIGEMINAL NEURALGIA ASSOCIATED WITH A SOLITARY DEMYELINATING PONTINE LESION: A CASE REPORT

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Background and Aims: Trigeminal neuralgia associated with brainstem lesions is currently considered as a rare condition and only few patients have been reported so far in literature. Tohyama and colleagues recently proposed the nosological entity of trigeminal neuralgia associated with solitary pontine lesion, trying to categorize it as a new clinical syndrome on its own. Based on this description, trigeminal neuralgia associated with solitary pontine lesion patients have an identical clinical presentation compared to other patients with trigeminal neuralgia but have a solitary pontine lesion. The nature of the pontine lesion has been attributed to several etiologies, including ischemia, demyelination or previous pontine viral neuritis. In those patients with a putative demyelinating lesion, a definite diagnosis of multiple sclerosis cannot be made due to the lack of dissemination in space. Very little is known in relation to the cerebrospinal fluid characteristics of this population of patients.

Methods: Case report

Results: We present a case of a 42-year-old man suffering of trigeminal neuralgia associated with solitary pontine lesion with a likely demyelinating etiology. The patient herein described had an atypical trigeminal neuralgia associated with a single pontine lesion comparable to those described by Tohyama and colleagues. The MRI characteristics of the lesion, along with the presence of oligoclonal bands in the cerebrospinal fluid, suggested a demyelinating etiology. Trigeminal neuralgia associated with solitary pontine lesion may be categorized as a possible manifestation of solitary sclerosis.

Conclusions: Future research need to reveal which features can predict the risk of conversion to clinically defined multiple sclerosis and which treatments modify this risk.
ICARIIN INHIBITS DEMYELINATION BY TARGETING THE PHAGOCYTIC ACTIVITY OF MICROGLIA IN CPZ-INDUCED DEMYELINATING MICE

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Background and Aims:: The phagocytosis of myelin debris by microglia may be the key step to the treatment of multiple sclerosis (MS). Our aim was to investigate whether the neuroprotective effect of Icariin (ICA) is achieved by promoting phagocytosis of myelin debris of microglia.

Methods:: Mice were fed with a diet containing cuprizone (CPZ) for 4 weeks to induce demyelination. Then, the debris of myelin marked by CFSE were injected into the unilateral corpus callosum in mice. Then, the mice were injected with ICA for two weeks. BV2 and bone marrow-derived macrophages were inoculated on the 6-well plate. After cell adherence, CFSE-labeled myelin debris and ICA were incubated. Relevant cytokines and proteins were detected by western blot, Immunofluorescence and ELISA.

Results:: Compared with normal mice, CPZ-fed mice showed extensive demyelination, which was inhibited by ICA treatment. The presence of CFSE-labeled myelin debris in microglia was observed under immunofluorescence, and the phagocytosis of myelin debris by microglia was enhanced by ICA intervention. Microglia mediated TREM2 receptors to promote phagocytosis, and partially affected the TLR4/NF-κB and Nrf2/HO-1 signaling pathways, reducing neuroinflammation and oxidative stress in the brain. The same result was verified in the in vitro BV2/BMDMs experiment, thereby promoting the repair of myelin sheath.

Conclusions:: ICA effectively promotes the phagocytosis of myelin debris by microglia, and reduces oxidative stress and inflammation, thereby inhibiting the loss of myelin. (NNSF of China 81473577, 81471412, 82004028; Natural Fund Project of Shanxi Province 201901D111334, 201901D211538; Shanxi University of Chinese Medicine 2018TD-012. Ma and Xiao are corresponding authors)
THE PSYCHOLOGICAL EFFECT OF COVID19 PANDEMIC ON NEUROMYELITIS OPTICA SPECTRUM DISORDER PATIENTS AND THEIR ATTITUDE CHANGE DURING THE PANDEMIC, AFTER A YEAR.

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Background and Aims:: Coronavirus 2019 is a new coronavirus that created a pandemic with high mortality. NMOSD patients are more affected by psychological effects of COVID19 pandemic such as anxiety since they may be worried to be prone to infection (due to the nature of disease and its treatment by immunosuppressants).

Methods:: The aim of study was to evaluate the anxiety and fear due to COVID19 infection 3 and 12 months after beginning of epidemic. Study was done in patients of NMOSD Clinic of Kashani hospital, Isfahan. We asked them if they are anxious or afraid of the pandemic subjectively. To investigate the objective level of anxiety, Hospital Anxiety and Depression Scale questionnaire was filled. Also we asked them about respecting general cautions and sanitary protocols to prevent infection. The steps repeated after nine months.

Results:: 120 patients (96 female) with mean age of 36.37±9.69 and mean duration of disease about 8.49±5.35 years enrolled. 96 patients (80%) experienced anxiety during the first 3 months of pandemic. The point is that their level of anxiety decrease significantly with the prolongation of pandemic and just 66 patients (55%) showed anxiety on the second survey. Respecting preventive majors increase in the same period (wearing mask from 86.66% to 100%, social distancing from 75% to 90%, hand washing from 85% to 91.66%).

Conclusions:: Along with pandemic prolongation, level of anxiety had been decreased gradually. But the level of alertness and attention is almost high because they respect the sanitary rules and preventive disciplines more. It should be considered that awareness must be preserved till the end of epidemic.
ANTI-HBS TITERS ARE NOT DECREASED AFTER TREATMENT WITH ORAL CLADRIBINE IN PATIENTS WITH MULTIPLE SCLEROSIS VACCINATED AGAINST HEPATITIS B VIRUS

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Background and Aims:: Oral cladribine is a novel treatment for Multiple Sclerosis (MS). It is a purine nucleoside antimetabolite analogue that incorporates into the DNA, resulting in single-strand breaks in DNA and apoptosis of replicating lymphocytes. Specifically, Cladribine induces limited depletion of CD4 and CD8 T subsets and a more marked depletion of memory B cell subsets. Therefore, natural and acquired humoral response against pathogens may be potentially impaired. The aim of this study was to assess longitudinal variation of antiHBs titers in patients with MS treated with Cladribine.

Methods:: Patients with MS treated with 1 cycle of Cladribine (3,5 mg/kg) and previously vaccinated against Hepatitis B virus (HBV) were enrolled. Anti-HBs titers were compared pre and after 12 months from Cladribine treatment. Total lymphocyte count was also analysed.

Results:: Among the 14 RMS patients (11 F, mean age 33,7 SD 7) enrolled, all had anti-HBs titers >10 mg/dl at baseline. Anti-HBs titer dropped below the reference value (<10 mg/dl) at 12 months after Cladribine only in 1 case. Pre-post Cladribine mean anti-HBs values were not significantly different considering the whole cohort (Wilcoxon-Mann-Whitney Test p=0,76). Four patients had grade 1 and 1 patient grade 2 lymphocytopenia at 12 months.

Conclusions:: Cladribine does seem to reduce humoral immune responses in subjects previously vaccinated against HBV, even in case of drug-induced lymphocytopenia. These results, if confirmed in larger populations, appear reassuring also for other vaccinations (i.e. COVID19). The low impact of Cladribine on plasma cells may explain such findings.
GINKGO K PROMOTES THE PHAGOCYTOSIS OF MYELIN DEBRIS BY ASTROCYTES VIA REBALANCING TLR4 AND ABCA1 SIGNALING PATHWAYS

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Background and Aims:: Ginkgolide K (GK), a novel compound extracted from Ginkgo biloba, showed the ability to protect myelin sheath via promoting the phagocytosis of myelin debris by astrocytes, but the potential mechanisms are unknown. Our aim was to investigate the cellular and molecular mechanisms of GK on the phagocytosis of myelin debris by astrocytes.

Methods:: Primary astrocytes were cultured, and purified from newborn mouse. After incubation with CFSE-labeled myelin debris under the presence or absence of GK (50 μg/ml) for 24 hours, phagocytosis of myelin debris by astrocytes was detected with SpectraMax iD3. Then, pretreated with LPS or glibenclamide for 2 hours, astrocytes were incubated with CFSE-labeled myelin debris under the presence or absence of GK again. Relevant cytokines and proteins were detected by ELISA, western blot and immunohistochemistry, respectively.

Results:: The results showed that astrocytes contained CFSE-labeled myelin, which triggered the activation of TLR4 and inflammation response. GK treatment improved the phagocytosis of myelin by astrocytes, accompanied by an inhibition of inflammatory cytokines and TLR4 signaling, but an enhancement of neurotrophic molecules and ABCA1 signaling. Pretreatment with LPS or glibenclamide resulted in decline of the phagocytosis of myelin by astrocyte, and GK treatment promoted myelin uptake by astrocytes after a pretreatment with LPS, but had no influence on myelin uptake after a pretreatment with glibenclamide.

Conclusions:: GK could effectively promoted the phagocytosis of myelin debris by astrocytes via rebalancing TLR4 and ABCA1 signaling pathway. (NNSF of China 81473577, 81971194. Ma and Xiao are corresponding authors).
FULMINANT ACUTE DEMYELINATING ENCEPHALOMYELITIS (ADEM) WITH COEXISTING CEREBRAL VENOUS SINUS THROMBOSIS (CVT) IN PREGNANCY – AN UNUSUAL PRESENTATION

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Background and Aims:: Acute demyelinating encephalomyelitis (ADEM) is commoner in children than in adults. Pregnancy, a pro-thrombotic state is known to cause cerebral venous sinus thrombosis (CVT). ADEM is rare in pregnancy and its diagnosis can be challenging. Both ADEM and CVT occurring simultaneously in pregnancy are rare. We report such an unusual case.

Methods:: A 20 year old female presented in the second trimester of her pregnancy with headache, right hemiparesis, seizures and rapidly deteriorating level of consciousness. Examination revealed right side hemiparesis with a Glasgow coma scale of 8 out of 15. MRI brain showed bilateral asymmetrical signal changes involving cortical and subcortical regions of the brain with no clear evidence of cerebral venous sinus thrombosis. She deteriorated over the ensuing days and a repeat NCCT brain showed diffuse cerebral oedema. As most of her routine investigations including blood, serum, urine, inflammatory markers, CSF studies, autoimmune encephalitis antibody panel and anti-phospholipid antibody screening were normal she was subjected to a craniotomy with brain biopsy.

Results:: She was treated with intravenous antibiotic, acyclovir, steroid and anti-coagulated with low molecular weight heparin. Because of the deteriorating clinical state her pregnancy was terminated. She finally succumbed to her illness in spite of all interventions. Post-mortem revealed extensive cerebral venous thrombosis and histology of the brain revealed features consistent with ADEM.

Conclusions:: Fulminant ADEM in pregnancy is rare and the clinical presentation can vary. High degree of suspicion and advanced imaging are needed for an early diagnosis. When fulminant ADEM occur simultaneously with CVT the prognosis is poor.
Background and Aims:: Neurofibromatosis type 1 (NF1) is an autosomal dominant neurocutaneous disease which confers an increased risk of malignant tumour. NF1 is one of the most common autosomal dominant genetic disorders. Relapsing remitting multiple sclerosis (RRMS) is an inflammatory demyelinating disease of the central nervous system. The coexistence of multiple sclerosis and NF1 is rare but has been reported. We describe the case of a man with NF1 and RRMS successfully treated with natalizumab.

Methods:: The coexistence of RRMS and NF1 is very rare but has been described in the literature. The patient was studied with contrast enhanced brain and spine MRI as well as lumbar puncture. Treatment option discussed.

Results:: MRI imaging showed multiple supra- and infra-tentorial demyelinating lesions. In addition, multiple focal alterations with both centromedullary and peripheral distribution in C1, C2, C5 and D3 in the cervical and dorsal spinal cord were seen. The CSF analysis showed presence of oligoclonal IgG bands. A formal diagnosis of MS was made. After a course of metilprednasonolone 1000mg i.v. for 5 days, therapy with intravenous natalizumab 300 mg every 6 weeks was started (JCV index above 1.5).

Conclusions:: Natalizumab therapy resulted in an excellent disease control with a 2 point reduction in the disability, while minimizing the risk of possible oncogenic effects on NF1 triggered by immunosuppressants. No relapses were detected at 24 months. Due to the elevated JCV index, a DMT shift may be needed in the short-term. This will expose patients to risk of MS rebound and challenge the physician decision-making process.
PREVALENCE OF INSULIN RESISTANCE AND DYSLIPIDEMIA IN MULTIPLE SCLEROSIS AND ITS CORRELATION WITH DISEASE ACTIVITY

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Background and Aims:: BACKGROUND Insulin resistance (IR) and dyslipidemia have been described as comorbidity in multiple sclerosis (MS) contributing to disease progression and disability. AIMS To study the prevalence of IR and dyslipidemia in a North Indian cohort of MS patients and its correlation with disease activity.

Methods:: METHODS Fifty relapsing remitting MS patients aged 15 – 55 years fulfilling the 2017 modified Mc Donald criteria and fifty age- and sex-matched healthy controls were recruited. Fasting blood glucose, insulin, glycated hemoglobin and lipid levels were done at baseline for all participants and at one year follow-up for patients. IR was calculated by Homeostatis Model Assessment (HOMA - IR). The disease activity and disability were assessed by magnetic resonance imaging (MRI) of brain and spinal cord using the demyelination disease protocol, and Expanded Disability Status Score (EDSS), respectively at baseline and after one year follow-up. Descriptive statistics was used.

Results:: RESULTS The mean age of patients was 32.3±7.9 years and mean BMI was 24.8±2.8 kg/m². The mean baseline EDSS was 2.8±1.4. The prevalence of IR and dyslipidemia were 70% and 92% of patients respectively. Low HDL was the most common abnormality seen in 82.6%(38/46) followed by raised levels of LDL seen in 60.9% (28/46) of patients. IR and dyslipidemia did not correlate with EDSS and MRI lesion load at baseline and at one-year follow-up.

Conclusions:: CONCLUSION Insulin resistance and dyslipidemia were prevalent among MS patients and did not correlate with disease activity.
OCRELIZUMAB TREATMENT IN MULTIPLE SCLEROSIS: PROSPECTIVE REAL WORLD OBSERVATIONAL MULTI-CENTER STUDY IN CAMPANIA, ITALY

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Background and Aims:: We aimed at exploring potential impact of early ocrelizumab introduction and its efficacy on disability accrual in multiple sclerosis patients.

Methods:: We included relapsing remitting or active secondary progressive MS patients treated with Ocrelizumab. Including patients with at least one-year follow-up we assessed the association between baseline clinical features and treatment efficacy through multilevel-mixed analysis.

Results:: We included 89 relapsing and 294 progressive patients (205 Female, mean age: 45.8 ± 11.2, disease duration: 12.7 ± 11.6 years), with 217 patients followed up for more than 12 months. Both relapsing and progressive patients showed an increased EDSS at baseline compared to the year before ocrelizumab start (coeff. = 0.18, 95%CI=0.30 – 0.34, p=0.02; coeff. = 0.28, 95%CI=0.18 – 0.37, p<0.001) while no further increase was observed after 1 year. Patients naive to DMTs showed a decreased EDSS one year after ocrelizumab treatment compared with EDSS at baseline (relapsing: coeff. = -0.29, p=0.02; progressive: coeff. = -0.33, p=0.01). Patients with a time from conversion shorter than 5 years showed an increased EDSS between one year before ocrelizumab start and baseline (coeff. = 0.42, 95%CI=0.12 – 0.72, p=0.005), with no EDSS increase in the following year (p=0.38).

Conclusions:: We observed that better responders to ocrelizumab were naïve patients and those with a time from conversion shorter than 5 years. The present study highlighted the need to treat patients as early as possible to be able to affect disease trajectory in the therapeutic window.
TRANSCUTANEOUS SPINAL CORD STIMULATION (TSDCS) IN MULTIPLE SCLEROSIS

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Background and Aims:: Multiple Sclerosis (MS) is a multifactorial disease of the Central Nervous System in which both inflammatory and neurodegenerative processes occur simultaneously. Over the past few years, several studies suggest positive effects of non-invasive neuromodulation in MS. We therefore aim to investigate in patients with MS the clinical effects of transcutaneous spinal direct current stimulation (tsDCS) and potential mechanisms of action on neuroinflammation through the assessment of biomarkers for oxidative stress and inflammation.

Methods:: 7 subjects (5 men; aged 42-70), with MS and spasticity were studied. We delivered anodal and sham tsDCS (2mA, x 20 minutes) once a day, for 5 days consecutively. One electrode was positioned over the spinal process of the tenth thoracic vertebra and the other above the right shoulder. In each session, clinical and biochemical measures were administered before the treatment (baseline), on day five (T1) and after 1 month (T2).

Results:: After anodal tsDCS our results showed a decrease of ROS production rate (umol.min⁻¹; p<0.05; -6%) and an increase in antioxidant Capacity (TAC; mM; p<0.05; +4%), while sham tsDCS failed to induce changes. Besides, an increase in total and reduced Glutathione (GSH; umol.L⁻¹) can suggest an antioxidant effect of DC current. At T2 Ashworth scale improved by about 42% and MS spasticity scale about 17%.

Conclusions:: Anodal tDCS, over the spinal process, seems to induce an antioxidant effect, in MS patients. This pilot study has demonstrated a possible therapeutic role of tsDCS. However, to confirm our data, a larger sample size is needed.
CLINICAL PREDICTORS OF THE BENIGN COURSE OF MULTIPLE SCLEROSIS IN A MEDICALLY UNDERSERVED POPULATION

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Background and Aims: Benign multiple sclerosis (MS) is characterized by little disability accumulation over the disease course. The majority of contributions to understanding the predictors of benign MS come from high-income areas; it is unknown whether the same predictors can be derived from the resource-limited populations that have limited access to proper diagnostics and management. We aimed to study clinical predictors of benign MS in individuals with relapsing-remitting (RR) course coming from underserved areas.

Methods: This retrospective study used clinical data of 55 residents of underserved areas with RR-MS with a minimal disease duration of 10 years. The benign course was defined as EDSS ≤ 3.0 after 10 years from MS onset. Binominal logistic regression was used to study the association between the benign course of MS and sex, smoking, diagnostic errors at disease onset, time to the establishment of the diagnosis, disease-modifying therapy, and EDSS, symptoms and age at MS onset.

Results: Of 55 patients (average disease duration 28.47±9.5 years), 16 (29%) had a benign course. Lower EDSS at onset was the only factor associated with benign RR-MS (OR 0.56, 95%CI 0.35-0.8, p=0.005).

Conclusions: EDSS at the disease onset was the only determinant of benign RR-MS course in our cohort; while this predictor is consistent with the available literature data, other factors turned to be nonpredictive, which may be explained by a small sample. Further studies are needed to address this question.
MRI CHANGES IN EARLY STAGES OF NMOSD AMONG THE POPULATION OF UZBEKISTAN

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Background and Aims:: Early diagnosis of Neuromyelitis optica spectrum disorders (NMOSD) is critical. Unlike multiple sclerosis, NMOSD episodes are normally quite severe. These episodes can lead to irreversible consequences. The diagnosis of NMOSD is based on the presence of evidence of optic neuritis and transverse myelitis. Study additional findings in early MRI scans could play important role in early diagnosing and treatment course.

Methods:: We retrospectively analyzed the results of MRI scanning among 45 patients in the Tashkent Medical Academy Neurology Department with a diagnosis NMOSD.

Results:: The results of MRI study demonstrated a high incidence of involvement of the brain stem (44%) and hemispheres periventricular white matter (21%) at the time of disease clinical debut. Lesions involving corticospinal tracts and diencephalic region was find only in one patient (2.2%).

Conclusions:: This study confirms that early MRI diagnosing results among patients with NMOSD in Uzbekistan usually demonstrate involve-ment of the brainstem and hemispheres periventricular white matter.
ETIOLOGICAL RESEARCH IN PEDIATRIC MULTIPLE SCLEROSIS: A TOOL TO ASSESS ENVIRONMENTAL EXPOSURES (PEQ-IT)

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Background and Aims:: Little is known about the environmental risk determinants in POMS, although evidences support an increased susceptibility related to a gene-environment interaction. An Italian multicenter case-control study (the PEDIGREE study) has been launched to investigate the environmental component and the PEDIGREE Questionnaire (PEQ-IT) aims to collect relevant information on past exposures in POMS. To better understand the role played by environment in determining POMS, a new validated tool is presented.

Methods:: PEQ-IT was developed through translation and adaptation of a questionnaire used in POMS U.S. studies and was tested for relevance, acceptability, feasibility and reliability through a pilot study. This phase was conducted in a population of pediatric subjects and their parents recruited from pediatric clinics and general population from five Italian participating sites.

Results:: PEQ-IT achieved good level of relevance, excellent levels of acceptability and feasibility, and reliability was rated as at least moderate in all sections.

Conclusions:: PEQ-IT represents an effective vehicle for collecting information on a potentially highly informative disease as to the role of environmental exposures in generating susceptibility to MS. Our results suggest that PEQ-IT should be administered through interview or in presence of the researcher, so as to ensure good quality of data. We believe that the development, pilot testing and dissemination of research tools could optimize efforts and ensure greater comparability of evidence in epidemiological research. The study received funds from the Italian Multiple Sclerosis Foundation (Fondazione Italiana Sclerosis Multipla, FISM, Genoa, Italy), grant n. Prot. N. 12/18/F14 (P.I. Angelo Ghezzi).
THE COVID-19-RELATED QUALITY OF LIFE CHANGES IN PATIENTS WITH MULTIPLE SCLEROSIS

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Background and Aims:: Multiple sclerosis (MS) is a chronic disease affecting the central nervous system. The aim of the study was to evaluate the quality of life (QOL) of patients with relapsing-remitting MS, who suffered from Covid-19 disease.

Methods:: Methods. We examined 48 patients (31 - women and 17 – men). The QOL was evaluated by the questionnaire SF-36. The mean age was 38 ± 18 years. The average disease duration was about 8.32 ± 11.54 years and the EDSS score was 3,1 ± 1.7. Confirmed Covid-19 was diagnosed in 27 of patients (PCR or retrospective IFA-test). The QOL results of those who had Covid-19 were compared to those who were not infected (control group).

Results:: Results. The SF-36 results were the following: physical functioning - (33,30 ± 2,33) points against (53,00 ± 3,67) in the control group (p <0,01), physical role functioning - (15,25 ± 2,57) and (61,73 ± 5,84) (p <0,01), bodily pain - (34,26 ± 1, 85) scores and (51,25 ± 5,48) (p <0,05), general health - (21,91 ± 1,36) points against (41,80 ± 2,64) ( p <0,05), vital activity - (41,43 ± 1,64) scores and (65,50 ± 2,34) (p> 0,05), social functioning - (52, 12 ± 1,80 points and (68,14 ± 3,81) (p> 0,05), emotional role functioning - (26,81 ± 3,08) and (48,02 ± 7, 42) scores (p <0,05), mental health - (31,54 ± 1,55) points against (51,44 ± 2,65) (p <0,05).

Conclusions:: Conclusions. Thus, a significant quality of life decrease was observed in all subscales except vital activity and social functioning.
Background and Aims:: Fatigue is recognized as a common symptom reported by patients with multiple (MS). His presence has created a new challenge in the management of these patients. Our objective was to assess the impact of fatigue on the various spheres of daily functioning, in particular the physical, cognitive and psychosocial spheres, and to demonstrate the relationship between fatigue and Expanded Disability Status Scale (EDSS).

Methods:: A retrospective study of 60 patients with MS was conducted at the Neurology Department of the Military Hospital of Tunis over a period of 14 years (2015-2019). The form of MS and the Expanded Disability Status Scale (EDSS) were collected. Fatigue was measured using the Fatigue Severity Scale (FSS). The physical, cognitive and psychosocial impact was assessed by the Fatigue Impact Scale (EMIF-SEP).

Results:: Among the 60 patients, 39 suffering from fatigue, with an average FSS score of 4.67. The mean score of EMIF-SEP is 65.36 / 100. Higher EMIF-SEP total scores were associated with higher EDSS. There were also higher physical and psychological subscale scores of EMIF-SEP linked to higher EDSS.

Conclusions:: Fatigue can interfere in daily functioning of patients with MS. This impact justifies the particular interest given to this symptom to find various management strategies.
Background and Aims:: Background and goals. The immune system dysfunction in MS patients are accompanied by the production of autoantibodies to neurotransmitters. The relationship between the level of AT to serotonin (ATC), norepinephrine (ATH), and histamine (ATG) and the clinical signs of MS was evaluated.

Methods:: The level of AT in the blood serum in conventional units (CU) of optical density was measured by a sensitive electro-optical method. Were examined 38 MS patients, control group (CG) of 20 patients with non-autoimmune diseases of the nervous system and 20 donors (D).

Results:: The level of ATG in MS patients was Me -0.452 CU, which is significantly higher than in the CG and D groups (p< 0.05). There was a significant increase in ATG to Me- 0.497+0.002 CU as a possible marker of inflammation in the period of recovery from exacerbation in the remitting course of MS. There was a statistically significant increase in the level of ATN in patients with MS Me-27.0 CU, in comparison with CG and D. The lowest ATN indicators are characteristic of: the stage of remission of MS Me-24.5 CU and in the group of MS with stress-inducing mechanisms of development Me-23.0 CU. The level of ATC in MS patients was Me-18.3 CU, which is 4.0-4.4 times higher than in CG and D. There was an increased level of ATC in MS patients with severe damage to the sensory system.

Conclusions:: The results indicate the significance of neuroimmunopathological disorders in MS and may be an additional marker of the clinical features of MS.
DISTURBANCE OF SEROTONERGIC REGULATION OF HEMATOPOIETIC STEM CELLS (HSCS CD 34+) AND BLOOD MONONUCLEAR CELLS (BMCS) IN PATIENTS WITH MULTIPLE SCLEROSIS (MS),

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Background and Aims:: Background and goals. Serotonin is involved in the mechanisms of regulation of the function of immunocompetent cells through the receptor apparatus. The aim of the study was to evaluate the expression capacity (EC) of BMCs and HSCs under the influence of serotonin - creatine sulfate at a dose of $10^{-4}$ M in the "in vitro" test system (TS). Violation of the receptor apparatus of cells serotonin led to a change in their quantitative registration.

Methods:: We studied BMCs by enzyme immunoassay and ELISA in 86 patients with MS and HSCs in 12 patients. The control group included 16 donors, 12 patients with autoimmune diseases and hemoblastosis (AD).

Results:: In contrast to MS patients, donors showed an increase in the EC of CD3+ and CD8+ cells under the influence of serotonin. In TS, there was a smaller increase of CD16+ cells (p<0.002) with a decrease in their expression capacity, and the number of CD20+ and CD56+ decreased. In TS, patients with AD had lower quantitative values in comparison with MS: CD3+, CD4+, CD8+ cells (p<0.05) MS, except for CD54+ cells. This may indicate the resistance of individual populations of MNCs in MS patients to serotonergic regulation, regardless of clinical signs. Similar phenomena were observed in the HSCs of MS patients. The calculated deviation coefficient in the HSCs test system was 0.12+0.15 at MS, -0.59+0.23 at AD (p<0.05), −0.25+0.4 in donors.

Conclusions:: The observed changes indicate a defect in the serotonergic regulation of BMCs and HSCs in MS and are probably systemic in nature.
THE ROLE OF D2-LIKE DOPAMINERGIC RECEPTORS IN DOPAMINE-MEDIATED MODULATION OF TH17-CELLS IN MULTIPLE SCLEROSIS.

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Background and Aims:: Dopamine participates in multiple sclerosis (MS) pathogenesis by modulating immune cell activity. This study aimed to clarify the role of dopaminergic receptors in dopamine-mediated modulation of Th17-cells in MS.

Methods:: Thirty-four MS patients and twenty-three controls were examined. To assess the effect of dopamine on Th17-cells, CD4+ T-cells were cultured in the presence of dopamine and stimulated with anti-CD3/anti-CD28-antibodies. To study the involvement of dopaminergic receptors in dopamine-mediated immunomodulation, CD4+ T-cells were pre-incubated with antagonists of D₁- or D₂-like dopaminergic receptors, whereafter dopamine and anti-CD3/anti-CD28-antibodies were added to the cultures. To assess the direct effect of D₂-like dopaminergic receptor activation on cytokine production, some samples of CD4+ T-cells were preincubated with a specific agonist of D₂-like dopaminergic receptors and stimulated with anti-CD3/anti-CD28-antibodies. The levels of IL-17, IFN-γ and GM-CSF in supernatants were assessed by ELISA.

Results:: The production of cytokines was comparable between the groups. Dopamine suppressed cytokine production in both groups (p<0.0001). Blockade of D₁-like dopaminergic receptors did not affect the influence of dopamine on cytokine production, while blockade of D₂-like dopaminergic receptors decreased dopamine-mediated suppression of IL-17, IFN-γ and GM-CSF production in MS patients (p<0.05). Finally, activation of D₂-like dopaminergic receptors reduced cytokine production in both groups (p<0.05).

Conclusions:: These data suggest an inhibitory effect of dopamine on Th17-cells in MS, which could be mediated by the activation of D₂-like dopaminergic receptors. This study was supported by grant from the Russian Science Foundation (project №19-75-00075).
PAROXYSMAL SYMPTOMS IN MULTIPLE SCLEROSIS

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Background and Aims:: paroxysmal symptoms are common manifestations of multiple sclerosis (MS). When established as the first clinical manifestation, they can easily be mistaken for transient ischemic stroke. The nature of these paroxysmal phenomena depends on their site of origin, which is usually in the brainstem or spinal cord. Our aim is: To diagnose multiple sclerosis based on atypical manifestations.

Methods:: A 23 year old male was admitted for dystonic movements that date back to 2 years before. The episodes consisted of sustained and involuntary muscular contraction of the right hemibody without facial involvement responsible for an abnormal attitude. A 32 year old female, with a history of postpartum thrombophlebitis of the lower limb, complained of heaviness of the lower limbs and dizziness occurring 1 to 10 times a day and lasting less than a minute. These episodes occurred since 6 months and disappeared after a month.

Results:: for the first patient: Brain MRI showed multiple lesions of the white matter, supra and subtentorial encompassing the corpus callosum, in periventricular and sub cortical regions, with ovoid and radial form, with hyper signal on FLAIR sequences. for the second patient, The brain MRI showed multiple lesions on the supra and infratentorial lesions in addition to the cervical medulla in which there was a gadolinium enhancement. for both, The MS was the most probable diagnosis.

Conclusions:: Establishing new criteria for diagnosing MS in the face of paroxysmal and infrequent symptoms is a dilemma for neurologists, especially for therapeutic management, which remains a paradigm.
Background and Aims:: Multiple Sclerosis (MS) may co-occur in subjects with coeliac diseases (CD). If MS belongs to the CD spectrum is not clear, equally if it shows specific clinical features.

Methods:: We retrospectively analyzed clinical, radiological and genetic variables in 18 MS+CD patients positive for serological, histological and genetic CD markers and 17 MS patients with risk factors for CD (CRF) such as being CD first-degree relatives or complaining CD symptoms, compared to 18 MS and 8 Neuromyelitis optica spectrum disorder (NMOsd) patients.

Results:: Optic neuritis (ON) and myelitis were the most common presentations at disease onset among MS+CD (38.89% and 50%) MS+CRF (24% and 41%) NMOsd patients (50% and 50%), compared to MS (11% and 28%). Using Kruskal-Wallis test and Bonferroni correction, a similar pattern was observed along the disease course for MS+CD compared to MS (84% vs 50%, p<0.011 for myelitis, 50% vs 22%, p=0.227 for ON). Predictive numbers of spinal cord lesions at MRI onset were higher in MS+CD and NMOsd compared to MS patients (p<0.001). Considering the whole population, using a Poisson distribution, HLA DQ2/DQ8 genotypes were significantly associated with myelitis (p<0.002).

Conclusions:: ON and myelitis characterize the clinical phenotype of MS+CD and MS+CRF patients. Screening for CD should be included in differential diagnosis work-up in case of newly diagnosed MS patients predominantly showing these clinical features. Further studies will clarify if MS associated with CD should be considered a new disease entity.
Background and Aims:: Multiple sclerosis is a chronic immune mediated demyelinating disorder involving the central nervous system. The familial recurrence rate is estimated at about 15% and rare in Asia. To the best of our knowledge MS occurring in a mother-son pair has not been reported before either from Sri Lanka or South Asia.

Methods:: Son: A 26 years old male presented with progressive difficulty in walking for 1 year. Examination revealed bilateral spastic paraparesis without sensory involvement and left cerebellar signs. Mother: A 43 years old lady had progressive limb weakness, gait instability and left side visual impairment for 10 years. Both son and mother fulfilled MAGNIMS 2016 MRI criteria and McDonalds 2017 criteria for the diagnosis of MS. Both son and mother were diagnosed with primary progressive MS. MRI of son (Figure 1), MRI of mother (Figure 2) and all other investigations (Table 1) are summarized.
Figure 1: MRI brain and spine of son; (A) T2 sagittal, (B) T2 FLAIR axial, (C) T1 axial images demonstrates numerous T2 high signal T1 low signal white matter lesions arranged perpendicular to the bilateral lateral ventricles suggesting Dawson’s fingers. Lesions involve the corpus callosum, callosal-septal interface and the posterior fossa.

T2 axial image of the orbits (D) shows right optic neuritis.

Cervical spine T2 sagittal (E) and axial (F) images demonstrate multiple short segment T2 high signal lesions without significant spinal cord edema and expansion. Lesions are not contrast enhancing.
Results:: MS is a chronic disabling disease, common among women and median age of onset is 28 to 31 years. Exact cause of MS is yet to be determined and several etiological factors including viral infections like EBV and genetic factors especially variation involving the HLA-DRB1 loci has been postulated. Familial MS is variable in some geographic locations and absent in some ethnic groups.

Conclusions:: MS is thought to be less prevalent in Sri Lanka and the true prevalence is yet to be determined. This case highlights the importance of obtaining a family history in MS and the possibility of MS to running in families.
WUZI YANZONG PILLS RELIEVE CPZ-INDUCED DEMYELINATION BY IMPROVING THE MICROENVIRONMENT IN THE BRAIN

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Background and Aims:: Wuzi Yanzong Pills(WYP) can be used to treat neurological diseases, but its therapeutic effect on multiple sclerosis(MS) is still unclear. To explore the effect of WYP on improving demyelination and its mechanism in the microenvironment.

Methods:: The male C57BL/6 mice were randomly divided into control group, model group and WYP group. The model group and WYP group were fed with 0.2% CPZ feed for 6 weeks, and WYP group was gavaged with WYP(16g·kg⁻¹·d⁻¹) at the end of second weekend, twice a day for 28 consecutive days. Luxol fast blue staining detected the degree of demyelination of the corpus callosum. Western blot detected the protein expression levels of Arg-1 and iNOS in the brain. ELISA detected the content of IL-6, IL-1β, IL-10 and TGF-β in the brain.

Results:: Compared with the control group, the average integral optical density of model group decreased(P<0.0001), the levels of iNOS, IL-6, IL-1β increased(P<0.05,P<0.01, P<0.001), while the levels of Arg-1, IL-10, TGF-β decreased(P<0.05, P<0.01).Compared with the model group, the average integral optical density of WYP group increased(P<0.0001), the levels of Arg-1, IL-10, TGF-β increased(P<0.05, P<0.0001), while the levels of iNOS, IL-6, IL-1β decreased(P<0.05,P<0.01, P<0.001).

Conclusions:: WYP can significantly improve CPZ-induced demyelination, its mechanism may be related to reducing the inflammatory environment in the central nervous system.(Grants: NNSF of China 81102552 and 81703978,Central Government Guided Local Funding Projects for Science and Technology Development YDZX20201400001483,Key Research and Development Projects of Shanxi Province 201803D31209,Shanxi University Science and Technology Innovation Project 2019L0724. *corresponding authors: Prof. C.G. Ma or Prof. H.J. Fan)
Background and Aims:: The clinical spectrum of MOG-IgG-associated disease has expanded from pediatrics with acute disseminated encephalomyelitis to adult patients presenting as NMO-SD. It is characterized by significant optic nerve damage and steroid responsiveness. Indian data on this new disease is insufficient. It is important to correctly diagnose it as its treatment strategy is different from other demyelinating diseases, particularly MS.

Methods:: 19 adult (Age >12 years) patients who presented to KEM hospital, Mumbai from August 2017 to January 2020 with NMO-SD and were seropositive for MOG-IgG antibodies were prospectively evaluated for clinical and radiologic spectrum and response to treatment.

Results:: 19 patients had 36 attacks. 61.1% (11/18) were males while 38.9% (7/18) were females. 50% (9/18) belonged to age group 20 years to 40 years, 38.9% (7/18) were from 12 years to 20 years age group and only 11.1% (2/18) patients were above 40 years of age. 22.2% (4/18) had only optic neuritis, 16.7% (3/18) presented with only LETM, 5.5% (1/18) with brainstem demyelination and 27.8% (5/18) with cortical lesions. 22.2% (4/18) had LETM and optic neuritis. 61.1% (11/18) had monophasic and 38.9% (7/18) had a relapsing course. 55.6% (10/18) patients had optic neuritis either alone or in combination with others. 22.2% (4/18) patients had bilateral optic nerve involvement. Patients with h/o recurrent episodes had no further episode on immunosuppression at mean follow up of 12 months.

Conclusions:: MOG-IgG associated disease is a novel NMO-SD. Optic neuritis is the most common presentation. Monophasic illness is more common than relapses suggesting better prognosis compared to other demyelinating diseases.
AN INTRIGUING CASE OF COMBINED CENTRAL AND PERIPHERAL DEMYELINATION

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Background and Aims:: It is extremely rare to see combined central and peripheral nervous system demyelination. We are reporting this case of central demyelination in a case of multifocal acquired demyelinating sensorimotor neuropathy (MADSAM). After thorough review of literature, it is the first case report from India.

Methods:: A 28 years old male presented with 1.5 months history of progressive right upper and lower limb tingling and weakness followed by left hand tingling. There was no history of bladder or cranial nerve involvement. On examination patient had distal more than proximal weakness of right upper and lower limb with right hand wasting. All the DTRs were diminished and bilaterally plantars were extensor. Bilateral greater auricular, ulnar and radial nerves were thickened. He had positive Rhomberg’s with no cerebellar signs. Gait was normal.

Results:: NCS was suggestive of asymmetric multifocal demyelinating sensorimotor polyneuropathy affecting all four limbs. CSF showed 124 mg% protein with no cells. MRI Brain and spine was done in view of extensor plantar response. There were T2/Flair hyperintense lesions in periventricular white matter and mildly contrast enhancing lesions in left occipital, cerebellum, pons, patchy in cervical and thoracic cord. CSF OCB was negative, IgG index was normal. Serum NMO antibody was negative. Patient improved with IV pulse steroid followed by 3 months course of oral steroids and is stable on azathioprine.

Conclusions:: This is an intriguing case of classical MS- like central demyelinating disease presenting with peripheral demyelination i.e. MADSAM. The pathophysiology needs to be determined.
SAFETY AND EFFECT OF DIMETHYL FUMARATE ON WHITE AND GREY MATTER PATHOLOGY IN PATIENTS WITH MULTIPLE SCLEROSIS

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Background and Aims: To evaluate the safety and efficacy of dimethyl fumarate (DMF), a disease-modifying drug for the treatment of relapsing-remitting multiple sclerosis (RRMS), on both white and cortical and deep grey matter (GM) pathology.

Methods: A 2-year prospective study was performed on 177 RRMS patients treated with DMF and 47 untreated age and sex-matched patients. Patients underwent clinical evaluations, including Expanded Disability Status Scale (EDSS) assessment and a 3T-MRI at baseline, after 12 and 24 months. White and grey matter lesion load, brain volume change (PBVC), global and regional cortical thickness and deep grey matter volume changes were calculated.

Results: One-hundred forty-seven patients treated with DMF completed the follow-up. No severe reactions occurred; 4 patients developed severe, not confirmed, lymphopenia (<500/mm³). DMF led to lower incidence of relapses (14% vs 40%, p < 0.001), disability accumulation (EDSS change 0.1 ± 0.4 vs 0.4 ± 0.5, p < 0.001) and reduced white matter (0.4 ± 0.9 vs 2.6 ± 1.9, p < 0.001) and cortical lesions (CL) accumulation (0.2 ± 0.6 vs 1.9 ±1.6, p < 0.001). Among treated patients, 71% reached the NEDA-3 status and 18% the NEDA-4 status (cut-off for PBVC of 0.4%), with a mean annual PVBC of -0.55 ± 0.21%. Global and regional thickness and volumes changes were lower in treated patients (p < 0.001). Cox regression analysis showed younger age (HR 0.96[0.93-0.99], p 0.03) and higher EDSS (OR 1.32[1.06-1.66], p 0.01) as predictors of disease activity. CL number associated with annualized PBVC (β-1.46x10^-4, p 0.0343).

Conclusions: A significant effect of DMF on the progression of both focal and diffuse GM damage was noticed.
Background and Aims:: WYP has a potential therapeutic effect on EAE Mice, but the mechanism is not clear. To investigate the therapeutic effect of WYP on EAE mice and its effect on ERS.

Methods:: Mice were randomly divided into normal, model and WYP groups. EAE model was established by MOG\textsubscript{35-55}. From the third day after immunization, 25 days of drug intervention. The neurological function scores were recorded daily. On the 28th day after immunization, the spinal cord samples of mice were collected. The infiltration of inflammatory cells and the degree of demyelination in spinal cord tissues were observed by hematoxylineosin staining and Luxol fast blue staining method. The expressions of GRP78, GRP94, p-PERK, p-IRE1\textalpha, p-JNK, Caspase-12 and CHOP were detected by Western blot. The expressions of ATF6\textalpha was detected by fluorescence PCR.

Results:: The model group of the neurological function score increased (P<0.05), the degree of inflammatory infiltration and demyelination increased (P<0.01), the expressions of GRP78, GRP94, p-PERK, p-IRE1\textalpha, ATF6\textalpha, p-JNK, Caspase-12 and CHOP increased (P<0.05, P<0.01). The WYP group of the neurological function score decreased (P<0.05), the degree of inflammatory infiltration and demyelination decreased (P<0.05, P<0.01), the expressions of GRP78, GRP94, p-PERK, p-IRE1\textalpha, ATF6\textalpha, p-JNK, Caspase-12 and CHOP decreased (P<0.05, P<0.01).

Conclusions:: The effect of Wuzi Yanzong Pill on EAE may be related to reduce the activation of ERS-mediated pro-apoptotic pathways by down-regulating sustained ERS response. (Grants: NNSF of China 81102552 and 81703978, Central Government Guided Local Funding Projects for Science and Technology Development YDZX20201400001483. *corresponding authors: Prof. C.G. Ma or Prof. H.J. Fan)
MICROBIOME SIGNATURE IN MULTIPLE SCLEROSIS IN NORTH INDIA

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Background and Aims:: Background: Gut microbiome dysbiosis has been associated with many disorders including Multiple Sclerosis (MS) through bi-directional gut-brain axis. In western studies, characterization of gut microbiota in MS is well established but the differential effect of Indian diet in disease process of MS is yet to be explored. This ongoing study aims to study the gut microbiome in North Indian MS patients. Objective: To characterize the gut microbiota in North Indian MS patients and correlate it with disease activity.

Methods:: Relapse remitting MS (RRMS) patients (both naïve and on-treatment with disease modifying therapies), 18-60 years of age are being recruited. Major inclusions are RRMS patients with an Expanded Disability Status Score (EDSS) < 5.5 and exclusions are progressive forms of MS and no associated comorbidities. Stool samples have been stored at -80°C for further processing for DNA isolation and microbiome characterisation by 16S rRNA sequencing. 10 ml blood sample for serum Neurofilament light chain (NfL) assessment and isolation of DNA for HLA (human leukocyte antigen) DR typing.

Results:: 74 RRMS patients and 43 healthy controls have been recruited for the study. Out of total, 61 (82.4%) are RRMS and 13 (17.6%) are Aggressive RRMS patients. The mean (SD) age is 34.50 (8.10) and male:female ratio is 1:2 for recruited RRMS patients. The interim results of this ongoing study will be presented.

Conclusions:: Conclusion: The results of the study will characterize the gut microbiota of North Indian MS patients and its association with Aggressive MS if any.
MYELIN OLIGODENDROCYTE GLYCOPROTEIN (MOG) ANTIBODY TITRES AND RETINAL DEGENERATION IN MOG-ASSOCIATED DISEASE: A SINGLE CENTRE ITALIAN STUDY

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Background and Aims:: Optical Coherence Tomography(OCT) features in patients with Myelin Oligodendrocyte Glycoprotein-antibody associated disease(MOG-AD) are poorly explored. We investigated MOGab titres and OCT features in a cohort of MOG-AD patients.

Methods:: We obtained OCT scans from MOG-AD patients referring to IRCCS Mondino Foundation(Pavia). Patients were divided in two groups, according to MOGab titres at disease onset: low-titre-LT(≤1:640) and high-titre–HT(≥1:1280). We retrospectively collected clinical characteristics at disease onset and compared retinal nerve fiber layer(RNFL) and ganglion cell layer(GCL) thicknesses among the two groups.

Results:: Our cohort was made up of 7 patients(male/female: 1/6). Mean age was 36 years(SD 10.2). At disease onset, optic neuritis(ON) occurred in 5/7 patients, and 2 patients experienced myelitis. Four/7 patients belonged to LT group. OCT was performed at a mean follow-up time of 5 years(SD 3.6) from disease onset. Mean RNFL thickness was similar between LT and HT(92.5 µm vs 92.1, respectively), while mean GCL was lower in the HT group(72 µm) vs. LT(81 µm). Considering 5 eyes with history of ON, mean RNFL and GCL thicknesses were lower in HT(RNFL 82.5 µm, GCL 70 µm) than in LT(RNFL 86 µm, GCL 77 µm). Among 7 unaffected eyes, RNFL thickness was similar between groups(96 µm in LT vs. 98 µm in HT), while GCL thickness was lower in HT(74 µm) than in LT group(84 µm).

Conclusions:: MOGab titres at disease onset are related to retinal damage, even in patients without history of optic neuritis, thus reflecting a subclinical neuronal degeneration. GCL parameter could be considered more reliable than RNFL in assessing retinal damage.
Background and Aims:: In Multiple sclerosis (MS) the “rebound” of disease is a well known phenomenon occurring after the withdrawal of sequestering therapies as Natalizumab or Fingolimod. Until now, we don't know if other treatments acting on B cells as Rituximab or Ocrelizumab, for the specific mechanism of action, could give a reactivation of the disease after the suspension. Here we present a case of MS patient that present a strong reactivation of disease at Rituximab withdrawal.

Methods:: A 51-year-old female patient diagnosed with multiple sclerosis in 2011 with right hemiparesis, sensory and bladder disturbances. Over time, disease activity required several therapeutic switches until arriving in March 2018 at rituximab with clinical stability. In January 2019 we have scheduled a switch from rituximab (off-label treatment) to ocrelizumab (on-label treatment) monitoring the recovery of CD20, usually slow. Surprisingly the CD20 B cells increased rapidly from December to January 2019 (3% to 8%) with clinical (difficulty walking, numbness of the breast line and urinary retention) and radiological (new MRI cervical T2 lesions with gadolinium enhancement) worsening. After pulse steroid therapy, she started ocrelizumab treatment with clinical and instrumental stability.

Results:: To date, no cases of multiple sclerosis rebound in patients treated with anti-CD20 after discontinuation of Rituximab due to rapid immunoreconstitution have been described in the literature.

Conclusions:: Further studies are needed to better understand and predict CD20 immunoreconstitution after discontinuation of Rituximab and Ocrelizumab.
POST PARTUM PSYCHOSIS AS THE INITIAL PRESENTATION OF MULTIPLE SCLEROSIS: A CASE REPORT

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Background and Aims:: Psychotic disorders (PD) with multiple sclerosis (MS) is rare and occurs with rates of 2–3% and they usually develop after the neurological signs of MS. They are mostly linked to the side effects of treatment with interferon beta-group immune modifiers. MS revealed with an episode of psychosis is a rare entity mainly post partum psychosis (PPP).

Methods:: A case report of an uncommon presentation of MS revealed by a post partum psychosis.

Results:: We report a case of a 35 years old woman with no history of psychiatric disorder or drug abuse who developed psychiatric symptoms 15 days after she gave born to a child starting with delusional ideas, behavioral dysfunction, auditory and visual hallucinations associated to headache and insomnia. The neurological examination was normal and the psychiatric origin was initially retained. She was treated with neuroleptics without any improvement. Cerebro-spinal MRI was then performed which showed periventricular and short cervical T2 and Flair white matters. Some lesions were enhanced after gadolinium injection. The immunological study of the CSF showed IgG oligoclonal bands and there was no clinical or biological sign for systemic disease. MS was then retained according to the criteria of MacDonald 2017 and she received methylprednisolone and interferon therapy, which resulted in improvements in her clinical conditions.

Conclusions:: PPP is a severe, but treatable form of mental illness that can happen ‘out of the blue’ to women without previous experience of mental illness but sometimes it can be a manifestation revealing an organic illness such as MS.
DIFFICULT DIFFERENTIAL DIAGNOSIS BETWEEN NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOSD) AND WERNICKE ENCEPHALOPATHY (WE). CASE REPORT.

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Background and Aims:: NMOSD and WE could share similar clinical and neuroradiological manifestations. Differential diagnosis is difficult when NMOSD occurs with area postrema syndrome or mental status changes and when T2 hyperintense lesions involve thalamus, hypothalamus, periventricular and periaqueductal regions [1,3]. The involvement of mammillary bodies in NMOSD is rare [2].

Methods::
We describe the case of a 67-year-old woman, with story of daily alcohol abuse, admitted to Neurology Unit with altered mental state, ataxia and progressive loss of consciousness. In the previous days she reported nausea and vomiting. MRI showed symmetric T2 hyperintensity in the periventricular regions of the third and fourth ventricles and mamillary bodies with contrast enhancement. CSF profile revealed lymphocytic pleocytosis without oligoclonal bands. The laboratory test showed hyponatremia and anti-ENA antibody (anti-RO-52, anti-RO-60 and anti-La). We suspected WE and started intravenous thiamine and sodium supplementation with good improvement in consciousness and ataxia, but residual anterograde amnesia, disorientation and disinhibited behavior.

Results:
18 months later she developed rapid progressive flaccid tetraplegia, dysphagia and respiratory failure. MRI demonstrated a T2-hyperintense lesion from medulla to C6 with ring enhancement and in the chiasm and optic tracts. The presence of AQP4-IgG in her serum confirmed the diagnosis of NMOSD.

**Conclusions:** This is an atypical case of NMOSD because the involvement of mammillary bodies is rarely seen in this disease, being instead a usual location for WE. Pleiocytosis in CSF and presence of anti-ENA antibody might suggest NMOSD. Early detection of AQP4 could be essential for a correct diagnosis, before a relapse occurs.

CASE SERIES: MULTIPLE SCLEROSIS CLINICAL ONSET AND RELAPSE AFTER SARS-COV-2 INFECTION.

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Background and Aims:: SARS-CoV-2 infection has been associated with several neurological disorders including encephalitis, stroke, demyelinating disorders. We report three patients with multiple sclerosis (MS) onset or with a relapse of MS, temporally correlated with SARS-CoV-2 infection. We hypothesize that SARS-CoV-2 infection, as previously reported for other viruses, could drive active inflammatory response that can contribute either to the onset of MS or its relapse.

Methods:: We tested anti-SARS-CoV-2 Spike Ags IgG and IgM and a cerebrospinal fluid (CSF) PCR for SARS-CoV 2. Patients underwent also to brain and spinal cord magnetic resonance imaging (MRI). In patients with MS onset, we also performed lumbar puncture, autoimmunity testing, virological screening and multimodal evoked potentials (EPs).

Results::

Two patients tested negative for SARS-CoV-2 PCR in CSF, while three tested positive for anti-SARS-CoV-2 Spike Ags IgG, and negative IgM, supporting recent infection. The MRI performed in two patients with MS onset, showed widespread bilateral subcortical and periventricular active lesions and cervical lesions. MRI performed in MS relapse, showed diffuse encephalic new lesions with contrast enhancement. EPs, virological and immunity testing resulted normal.

Conclusions:: Viral infections are possible factors associated to MS pathologic mechanisms or triggers for MS. Extracellular vesicles are involved in cell-to-cell communication, also in blood-brain barrier (BBB) and macrovesicles (MVs) and exosomes in viral infection and antiviral response. Exosomes in SARS-CoV-2 infection, transfer ACE2 receptor to cells, supporting virus internalization. MVs promote BBB damage through co-involvement of tumor necrosis factor-α and interleukin-6. Resulting therefore,
plausible that SARS-Cov2 infection could drive the inflammatory response causing demyelinating disease.
BEHAVIOR OF LYMPHOCYTARY SUBPOPULATIONS DURING TREATMENT WITH DIMETHYL FUMARATE IN PATIENTS WITH MULTIPLE SCLEROSIS

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Background and Aims:: The appearance of Progressive multifocal leukoencephalopathy (PML) is a known risk associated with the use of Tecfidera, already described in its technical data. Its incidence is very low, but it is a disease with an unfortunate clinical course that can lead to death or produce severe disability of the patient.

Methods:: Dimethyl fumarate (DMF) is indicated as a disease-modifying treatment for patients with relapsing-remitting multiple sclerosis (MS R-R). It is a highly effective drug widely used among patients with R-R MS. Due to its mechanism of action DMF can cause lymphopenia.

Results:: To date, the risk of developing PML with the use of DMF was only associated with lymphocyte values below 0.5 x 10⁹ / L (severe lymphopenia) for a prolonged period (minimum 6 months). However, cases of PML with lymphocyte values > 0.5 x 10⁹ / L have been reported. In these cases, the absolute lymphocyte count may be close to normal, suggesting that other specific changes may occur in the T-CD4⁺ and specially in T-CD8⁺ lymphocyte subpopulations that favor the appearance of PML.

Conclusions:: This review attempts to update the scientific evidence about lymphopenia and the behavior of lymphocyte subpopulations in patients receiving DMF and whether there is a relationship with PML cases. It could be reasonable to particularize some cases and proceed to monitor lymphocyte subpopulations in patients with a higher risk of developing PML, such as: elderly patients, patients with lower lymphocyte counts since the start of treatment and patients previously treated with Natalizumab.
LYMPHOPENIA IN PATIENTS WITH MULTIPLE SCLEROSIS TREATED WITH DIMETHYL FUMARATE: A SINGLE-CENTER EXPERIENCE.

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Background and Aims:: Lymphopenia is a common side effect of treatment with dimethyl fumarate (DMF) in patients with multiple sclerosis (PwMS). The real prevalence and predictive factors of this side effect are still matter of debate.

Methods:: We retrospectively recruited PwMS that were treated for at least one month with DMF and collected clinical, demographic data and absolute lymphocyte count (ALC) during follow-up. Lymphopenia was graded according to CTCAE. We divided patients according to the grade of lymphopenia (all grades) and severe lymphopenia (grade II-IV). Characteristics of patients with/without lymphopenia and patients with/without severe lymphopenia were analyzed in order to highlight any statistical differences, then a logistic binary regression was performed to elucidate any predictive factor of lymphopenia and severe lymphopenia.

Results:: 98 patients treated with DMF were included: 46.9% of them developed lymphopenia, and 27.6% severe lymphopenia. Lymphopenia was associated with basal ALC (p<0.001), treatment duration (p=0.01), % of reduction at third month (p=0.001) Severe lymphopenia was associated with basal ALC (p=0.003).

Conclusions:: Lymphopenia is a common side effect of DMF. Basal ALC seems to be the most relevant predictive factor.
META-ANALYSIS OF METABOLIC BIOMARKERS FOR MULTIPLE SCLEROSIS IDENTIFIES NOVEL UPSTREAM REGULATORS

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Background and Aims:: Metabolomics holds promise as a non-invasive tool for revealing biochemical pathways implicated in multiple sclerosis (MS) (1). Specifically, Ingenuity Pathway Analysis (IPA) can be used to identify pathways associated with proteins and metabolites of relevance in MS as biomarkers or targets of intervention (2).

Methods:: We compared metabolite levels from biological fluids between MS patients and controls by performing Core Analysis in IPA. We included metabolites described as potential MS biomarkers in the literature. Each metabolite was associated with a 10-fold increase, when upregulated in MS, with a 10-fold decrease, when downregulated, or was considered unchanged, when found with conflicting or uncertain activation states.

Results:: Although no canonical pathway was significantly up- or down-regulated, several pathways likely play a role in MS, including those involved in the overproduction of free radicals, glutamate excitotoxicity and mitochondrial dysfunction (Figure). In the upstream analysis, which identifies molecular regulators of metabolite expression, huntingtin emerged as an upregulated upstream regulator, while curcumin appeared as an inhibited upstream regulator.

Conclusions:: Our findings indicate that metabolic pathways of huntingtin and curcumin may be relevant in MS pathogenesis. Upregulated huntingtin may have a pleiotropic role both in neuroinflammation, by regulating macrophage function and its response to stress (3), and in prevention of neurodegeneration, being involved in neuronal function and survival (4). The curcumin pathway, downregulated in MS, is typically involved in the antioxidant response to xenobiotics and stressful agents (5). We suggest that several metabolic processes remain to be explored in MS that may help to develop new, targeted treatment
strategies.
MULTIMODAL EVOKED POTENTIALS INFLUENCE MULTIPLE SCLEROSIS PHENOTYPE AND DISABILITY ACCRUAL

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Background and Aims:: Previous studies have suggested that Evoked Potentials (EPs) correlate with Multiple Sclerosis (MS) phenotype and disability rate. The goal of this study is to investigate whether multimodal EPs have distinct features between primary progressive (PPMS) and relapsing MS (RRMS) and are predictors of disability accrual.

Methods:: A comparative study was conducted in the department of Neurology of Razi Hospital including patients diagnosed with MS. Patients were relapse free at the time of neurophysiological assessment. They were divided into two groups: RRMS versus PPMS, matched according to disease duration. Data regarding visual (VEP), somatosensory (SSEP) and brainstem (BEP) evoked potentials were compared. Disability accrual was measured by the MS severity score (MSSS). P value<0.05 was considered as statistically significant.

Results:: Sixty-four patients were included (32 RRMS, 32 PPMS (sex-ratio=2.2)) and matched according to disease duration (9 years; p=0.9). VEP were impaired among 24/32 patients in PPMS versus 21/32 in the RRMS group (p=0.4). An axonal damage on optic nerve was found in three cases (PPMS=2; RRMS=1). SSEP were impaired in 21/22 cases in PPMS versus 12/24 in the RRMS group (p=0.001) with a predominant alteration in lower limbs (30/46). BEP were normal among 12/12 patients with PPMS versus 12/14 in the RRMS group (p=0.1). MSSS were significantly higher for patients with abnormal SSEP (2.2 versus 6.2; p=0.000) regardless of phenotype.

Conclusions:: Somatosensory pathways alterations are common during PPMS and are associated with disability accrual. This finding is due to a higher frequency of spinal cord lesions affecting the long tracts during this condition.
GWAS-ASSOCIATED VARIANTS, NON-GENETIC FACTORS, AND TRANSIENT TRANSCRIPTOME IN MULTIPLE SCLEROSIS ETIOPATHOGENESIS: A COLOCALIZATION ANALYSIS

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Background and Aims:: A clinically actionable understanding of multiple sclerosis (MS) etiology goes through GWAS interpretation, prompting research on new gene regulatory models. We previously suggested a stochastic etiologic model where small-scale random perturbations could reach a threshold for MS development. The recently described mapping of the transient transcriptome (TT), including intergenic and intronic RNAs, seems appropriate to verify this model through a rigorous co-localization analysis.

Methods:: Through Phyton and R, we performed a colocalization analysis of: (1) 601Multiple Sclerosis associated variants from GWAS Catalog; (2) selected MS-relevant human and EBV transducer DNA Binding Regions (DBRs), namely EBNA2, EBNA3C, AID, VDR; and (3)more than 4,5 million genomic intervals plausibly coding for transient RNAs (TrRNAs), including enhancers and super enhancers, sorted by the cell type and other experimental settings used in wet experiments from databases.

Results:: We show that genomic regions coding for the transient transcriptome are significantly enriched for MS-associated GWAS variants and DNA binding sites for molecular transducers mediating putative, non-genetic, etiopathogenetic factors for MS (vitamin D deficiency, Epstein Barr virus latent infection, B cell dysfunction).

Conclusions:: Our results suggest a model whereby TT-coding regions are hotspots of convergence between genetic ad non-genetic factors of risk/protection for MS (and plausibly for other complex disorders). We also set-up a freely available data resource at www.mscoloc.com for future research on transcriptional regulation in MS.
USE OF ALEMTUZUMAB IN A REAL-WORLD CLINICAL SETTING: THE EXPERIENCE FROM SAN RAFFAELE HOSPITAL

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Background and Aims:: Multiple sclerosis (MS) is an inflammatory disease of the central nervous system. Alemtuzumab (ALEM) is an immunosuppressant for highly-active (HA) MS. We present efficacy/safety profile of ALEM in a real-world setting.

Methods:: Data were collected from clinical records at San Raffaele Hospital.

Results::

<table>
<thead>
<tr>
<th>N=63 (F=40; 63,5%)</th>
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<tr>
<td>Age at ALEM start (y), mean ± SD (min-max)</td>
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<tr>
<td>MS Duration (y), mean ± SD (min-max)</td>
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<tr>
<td>EDSS, median (min-max)</td>
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<tr>
<td>1 year baseline ARR, mean (min-max)</td>
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<tr>
<td>2 year baseline ARR, mean (min-max)</td>
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<tr>
<td>Time from onset to ALEM start (y), mean ± SD (min-max)</td>
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Treatment characteristics

| T2-weighted lesion count pre ALEM start, number (percentage) | >9 lesions = 50 (79,4%) |
| Previous treatments, mean (min-max) | 2,5 (1.6-6) |
| Switch from 1st line DMDs, number (percentage) | 16 (38,1%) |
| Switch from 2nd line DMDs, number (percentage) | 28 (61,9%) |

| Number of patients with Gadolinium-enhancing lesion pre ALEM start, number (percentage) | 48 (76,2%) |

| Retreatment (II cycle), number (percentage) | 56 (88,9%) |
| Follow-up (y), mean ± stand dev (min-max) | 3,7 ± 1,6 (0,1-6,3) |

Table 1. Demographic clinical and neuro-radiological characteristic of population at baseline. Table legend: N= number of subjects included in the study, F= number of females, y= years, SD= standard deviation, min=minimum, max= maximum, MS= Multiple Sclerosis, EDSS= Expanded Disability Status Scale, ARR= Annualized Relapse Rate, ALEM= alemtuzumab, DMD= Disease Modifying Drug, m=months
Table 1 shows demographic, clinical and neuroradiological baseline characteristics of our cohort (63 patients). 88.9% received second ALEM-course and two patients did not for severe dysthyroidism and persistent disease activity after first cycle. Mean Annualized Relapse Rate (ARR), median Expanded Disability Status Scale (EDSS) and magnetic resonance imaging (MRI) activity at 24 and 36 months of follow-up are summarized in Figure 1. 49 patients had at least 24 months of follow-up and 53.1% reached No Evidence of Disease Activity (NEDA-3). 24.5% showed EDSS progression and 3 subjects underwent a third ALEM-course for disease activity. Table 2 shows ARR, EDSS and MRI activity at 24 and 36 months of follow-up in naïves. 18 had at least 24 months of follow-up and 72.2% reached NEDA-3. 25% showed mild/moderate infusion reactions and 2 subjects allergic reactions, which led to adoption of desensitization protocol for retreatment. 36.5% developed dysthyroidism, which needed...
radioiodine metabolic treatment in one case. Two patients developed Listeria Monocytogenes sepsis, one autoimmune hemophilia and one Fisher-Evans syndrome.

**Conclusions:** ALEM efficacy/safety profile in our cohort is comparable to clinical trials data. HA naïves with younger age, shorter MS history and lower EDSS score seemed to benefit more from ALEM. Further data and longer follow up are needed to confirm our observations.
CO-OCCURRENCE OF MULTIPLE SCLEROSIS AND AMYOTROPHIC LATERAL SCLEROSIS: A CASE REPORT

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Background and Aims:: Multiple Sclerosis (MS) is an immune-mediated, demyelinating and neurodegenerative disorder of the central nervous system. Amyotrophic Lateral Sclerosis (ALS) is a progressive neurodegenerative disorder that involves motor neurons in the cerebral cortex, brainstem and spinal cord. We report the co-occurrence of both MS and ALS within the same patient.

Methods:: Case report

Results:: A 52-year-old man was known by our Department of Neurology for MS diagnosed 21 years before, for which he was on treatment with Interferon-β. At the time of diagnosis, he presented left leg weakness and ataxic gait. Over the subsequent 20 years, his clinic-radiological findings were stable. In September 2019, he began to complain of worsening of weakness in his left leg, so he was treated with corticosteroids, without benefits. His lower limb weakness progressively worsened, eventually making him wheelchair-bound. In June 2020, fasciculations were evident on the tongue and the limbs that were also atrophic; there was paraplegia, hyposthenia on the left arm, dysarthria, dysphagia and dyspnea. The lesion burden was unchanged on MRI. Nerve conduction studies were normal, but there was widespread denervation on EMG, which confirmed a diagnosis of ALS. The genetic screening was negative. The patient rapidly deteriorated and died of respiratory failure within a month.

Conclusions:: Co-occurrence of MS and ALS has been reported in the literature for a few cases1 and a clear relationship has not been found as yet2-3. Searching for a link between the two conditions may shed light on their pathophysiologies, contributing to the development of more targeted therapeutic strategies.
BACKGROUND AND AIM:

Multiple sclerosis (MS) damage develops differently between the sexes. Here we investigate the relationship between cerebral grey matter (GM) hypoperfusion and white matter lesion volume and test whether this is different between the sexes. We hypothesize that there is a relationship between cerebral grey matter hypoperfusion and white matter damage and expect that this is affected by sex.

METHODS:

We recruited 94, clinically stable, relapsing remitting MS (RRMS) patients (M=27, F=67). In each patient, we calculated the proportion of T2-hyperintense lesion volume (T2LV) that is also hypointense on the T1-weighted images (T1LV), i.e., T1/T2 LV ratio. Global GM cerebral blood flow (CBF) was quantified using multi-inversion time pulsed ASL. For statistical analysis we used FSL tools, Pearson’s correlation and Wilcoxon test.

RESULTS:

CBF was negatively associated with T1LV ($r=-0.28$, $p=0.01$) and with T1/T2 LV ratio ($r=-0.39$, $p<0.001$) (Figure 1). There was no relationship between CBF and T2LV. There was no difference in T1LV and T2LV between men and women. T1/T2 LV ratio was different between the sexes ($p=0.005$), being higher in men. Women showed a correlation between CBF and T1/T2 LV ratio ($r=-0.3$, $p=0.01$) (Figure 2); this correlation was not significant in men ($r=-0.053$, $p=0.8$).
Conclusions:: Our results confirm a relationship between GM hypoperfusion and WM damage\(^5\) and suggest that an altered energy supply may play a role in the evolution of damage, and thus potentially in the progression of the disease, that is different in the two sexes.

Figure 2 (A) Sex differences in T1-hypointense and T2-hyperintense lesion volumes and in the T1/T2 ratio. (B) Correlations between CBF and T1/T2 ratio in women and men with MS.
Bladder Dysfunction in Multiple Sclerosis: A Preliminary Data from an Ongoing Hospital Based Study

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Background and Aims:: Bladder dysfunction in multiple sclerosis (MS) is common and is often overlooked. This could be due to dysfunction in bladder storage, voiding or both.

Methods:: Patients with MS diagnosed according to 2017 McDonald criteria who attend the MS clinic at the national hospital of Sri Lanka, with bladder symptoms were evaluated. Details on bladder symptoms, disease course and MRI were obtained. The Actionable questionnaire on quality of life in MS patients with bladder dysfunction was administered. An USS KUB with pre and post void bladder volumes and free flow uroflowmetry were performed. Treatment was commenced according to the type of bladder dysfunction with antimuscarinics and alpha blockers. The same questionnaire and QOL assessment were repeated after 10 weeks.

Results:: Out of eleven patients, three were (27%) males and 8 (72%) were females. The average EDSS of the group was 4. Three patients had hypotonic non-compliant bladder without outlet obstruction, five had hypotonic non-compliant bladder with outlet obstruction, two had normal detrusor with sensory urgency and one had bladder outlet obstruction only. Majority of the patients had bladders with no risk to upper tracts. The mean actionable symptom screening scores pre- and post-treatment were 16 and 9 respectively (P= 0.0014). 91% patients had demyelinating plaques in the cervical and dorsal spine on MRI.

Conclusions:: Bladder dysfunction in MS should be actively evaluated. Both storage and voiding dysfunction were observed in combination. Targeted treatment according to the type of bladder dysfunction significantly improved the symptoms and the quality of life.
CARDIOVASCULAR RISK IS ASSOCIATED WITH VERBAL LEARNING DYSFUNCTION IN MULTIPLE SCLEROSIS

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Background and Aims:: Cardiovascular comorbidities have been associated with cognitive decline in the general population. We evaluated the associations between cardiovascular risk and neuropsychological performances in MS.

Methods:: This is a cross-sectional study, including 69 MS patients. For all patients, we calculated the Framingham risk score, which provides the 10-year probability of developing macrovascular disease, using age, sex, diabetes, smoking, systolic blood pressure, and cholesterol levels as input variables. Cognitive function was examined with the Brief International Cognitive Assessment for MS (BICAMS), including the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test-II (CVLT-II), and the Brief Visuospatial Memory Test-Revised (BVMT-R).

Results:: Each point increase of the Framingham risk score was associated with 0.21 lower CVLT-II score. Looking at Framingham risk score components, male sex and higher total cholesterol levels were associated with lower CVLT scores (Coeff=-8.54; 95%CI=-15.51, -1.57; p=0.017; and Coeff=-0.11; 95%CI=-0.20, -0.02; p=0.015, respectively). No associations were found between cardiovascular risk and SDMT or BVMT-R.

Conclusions:: Cardiovascular risk is associated with verbal learning dysfunction in MS. Lifestyle and pharmacological interventions on cardiovascular risk factors should be considered carefully in the management of MS, given the possible effects on cognitive function.
PSYCHOLOGICAL CONSEQUENCES OF COVID-19 PANDEMIC ON PEOPLE WITH MULTIPLE SCLEROSIS: A META-ANALYTIC STUDY

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Background and Aims:: Covid-19 pandemic had a relevant psychological impact on consequences in medical workers and general population (Luo et al., 2020). The aim of the present meta-analysis was to evaluate the psychological consequences of Covid-19 pandemic in people with Multiple Sclerosis (pwMS), who are at higher risk of psychological distress than age-matched healthy controls (HC) (Boeschoten et al., 2017).

Methods:: The literature search on three electronic databases yielded 86 studies (73 after the removal of duplicates). Six studies compared psychological variables between pwMS and HC during the pandemic and six studies evaluated the pre/during the pandemic differences in pwMS. The following outcomes were selected: depression, anxiety, physical QoL, mental QoL, stress, sleep. Mean weighted effect sizes (ES) were calculated using Hedges’ g, via Prometa3 software.

Results:: During the pandemic, pwMS showed higher levels of depression (g=0.58, p=0.001), anxiety (g=0.49, p=0.047), stress (g=0.51, p=0.016) and sleep disturbances (g=0.46, p<0.001) compared to HC. The comparison on psychological outcomes before and during the pandemic in pwMS revealed no significant increase during the pandemic on levels of anxiety (g=0.15, p=0.161), depression (g=0.04, p=0.535), mental QoL (g=-0.14, p=0.060), and physical QoL (g=0.00, p=0.986), whereas sleep quality deteriorated during the pandemic (g=0.52, p<0.001).

Conclusions:: In accordance with studies carried on before the pandemic, pwMS showed higher levels of psychological distress than HC also during the Covid-19 pandemic; however, longitudinal studies revealed that, in pwMS, the only psychological consequence was ascribed to a reduced sleep quality. More studies are needed to evaluate the long-term consequences of the pandemic on pwMS.
COVID-19 IN MULTIPLE SCLEROSIS: EXPERIENCE FROM NORTH INDIA

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Background and Aims:: Background: Multiple Sclerosis (MS) patients on disease modifying therapies may be at risk of infection related to novel coronavirus disease (COVID-19) pandemic. Data on COVID 19 infections in Indian MS patients has not been well described Objective: To determine the clinical characteristics and outcome in MS patients on disease modifying therapies (DMTs) affected with COVID-19 and to assess the influence of COVID-19 infection on Multiple Sclerosis disease activity.

Methods:: Methods: Data was collected from our in-hospital MS registry between August to November 2020. Adult MS patients of any gender, subtypes with confirmed COVID-19 diagnosis based on a positive report of a SARS-CoV2 polymerase chain reaction were included. For each the Expanded Disability Status Score (EDSS), COVID-19 severity score and clinical outcome were assessed and patients followed up after a month.

Results:: Results: 5 Relapse RemittingMS (RRMS) patients with no comorbidities, on various DMTs with mean (SD) age 35.60(13.94), male: female ratio=3:2 and mean disease duration (years) 6.52 (3.42) were included in the study. 4 (80%) had COVID-19 severity score below 3. Median EDSS was 4 (range, 1-5.5). 1 (20%) was hospitalized. After one month of follow-up, median EDSS was 4.5 (range, 1-6), 1 (20%) had worsening of MS related symptoms (reported relapse) and 4 (80%) had positive COVID-19 IgG. No significant correlation was found between COVID-19 severity score, age, EDSS and disease duration (P>0.05).

Conclusions:: Conclusion: Indian MS patients were not at an additional risk of developing severe COVID 19 infection despite being on DMTs and COVID 19 did not influence MS disease course.
HHV-6 INFECTION AND ANTI-MOG ASSOCIATED MENINGOENCEPHALOMYELITIS IN AN IMMUNOCOMPETENT ADULT PATIENT

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Background and Aims:: A 42-year-old male patient was admitted with a clinical suspicion of acute transverse myelitis (TM). In about 24h he developed urinary retention, a lower thoracic (T8) sensory level and flaccid paraparesis.

Methods:: Routine blood laboratory showed mild lymphocytopenia and elevated inflammatory markers. Serum microbiological tests were negative for active infection (no IgM or DNA copies for CMV and EBV; all-encircling serological tests were all negative). Lumbar puncture showed 124 cells/uL (77% lymphocytes), high level of proteins (142 mg/dL, CSF Ig 10.7 mg/dL, liquor/serum albumin ratio 20.8, link index 0.6), with no OCB and a negative microbiological panel, except for isolation of HHV-6 (33851 copies/ml), with a lower serum viral titre (13414 copies/ml). MRI showed signs of meningoencephalomyelitis with a prominent medullary involvement.

Results:: Ganciclovir and dexamethasone (8mg bid) were started, with no benefit on clinical manifestations and CSF viral copies (33298 copies/ml) after 14 days. Meanwhile, further causes of TM were investigated and a dysimmune genesis was suspected. High dosage steroid was soon started and later Ig (0.4 g/kg/day) associated with prednisone (1 mg/Kg) was introduced, with progressive clinical improvement. Anti-MOG were found at high titer in serum and CSF, thus supporting our hypothesis. Genomic analysis of HHV-6 integration in hair samples confirmed an inherited chromosomally integrated viral genome.

Conclusions:: After 20 days, the patient recovered the ability to walk independently, with residual mild hypoesthesia in lower limbs and mild urinary symptoms (EDSS 2.5). After 6 months, MRI showed no signs of disease activity and the patient is clinically stable with maintenance therapy.
THE EVOLUTION OF COGNITIVE IMPAIRMENT IN MULTIPLE SCLEROSIS: A LONGITUDINAL STUDY

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Background and Aims:: Multiple sclerosis (MS) is the most significant cause of non-traumatic disability in young patients, due to the importance of its motor disability. Although neglected, cognitive impairment (CI) is a common feature that causes serious economic and social problems. We aimed to investigate the evolution of impairment within different cognitive domains in MS patients.

Methods:: A longitudinal study was conducted over 3 years recruiting MS patients from our department of neurology. Exhaustive neuropsychological assessment was performed, using the minimal assessment of cognitive function in MS (MACFIMS) and the French cognitive battery (BCcogSEP), at baseline and 3 years later, in order to evaluate the frequently affected cognitive domains and to determine the evolution of CI in MS.

Results:: Thirty MS patients were recruited (M/F=0,25). On average, the age at onset of the disease was 26,8 years, while the age at onset of CI was 30,6 years. Most patients (55%) were having 2nd line treatment, while 36% were treated with interferon. The information processing speed (IPS), working memory, and visuospatial functions were the most severely affected cognitive domains (93%). Less frequently, CI affecting attention skills (81%), executive functions (50%), and episodic memory (37%) were noted. Three years later, an alteration of the majority of the scores was observed, relating significantly to visuospatial functions, working memory, and IPS(p<0,05). These disturbances were significantly correlated to disability(p<0,05), but not correlated to MS treatment.

Conclusions:: We highlight the importance of early detection of CI in MS in order to improve care and minimize its impact on this young active population.
ACUTE DISSEMINATED ENCEPHALOMYELITIS ASSOCIATED WITH ANTI-MYELIN OLIGODENDROCYTE GLYCOPROTEIN (MOG-IGG) ANTIBODY IN A PATIENT WITH RECENT VACCINATION AGAINST SARS-COV-2

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Background and Aims:: Vaccines are one of the greatest achievements of modern medicine and are safely administered, but they can give rise to autoimmune diseases which include Central Nervous System or trigger/exacerbate chronic diseases such as multiple sclerosis, neuromyelitis optic and Myelin Oligodendrocyte Glicoprotein Antibody Disease (MOGAD). The SARS-CoV 2 is a human respiratory virus with neuroinvasive and neurotropic capabilities. Several SARS-CoV-2 vaccines have been developed, some with messenger RNA and other with viral vectors.

Methods:: We describe a case of encephalomyelitis with anti-MOG-IgG antibody and recent SARS-CoV-2 vaccine

Results:: A 51-year-old woman with no significant medical history presented with acute urinary retention and bilateral hypoesthesia with a T10 sensory level two week after the SARS-CoV-2 vaccine with viral vector. Magnetic resonance imaging showed enhancing T2 hyperintense lesions in the spinal cord with longitudinal extension, in the midbrain and in the optic nerves bilaterally. Serum SARS-CoV-2 IgG anti spike protein was positive (titer was 86 and cutoff 50 UA/ml). Nasopharyngeal SARS-CoV-2 PCR was negative. Cerebrospinal fluid analysis showed lymphocyte pleocytosis (50 cells/μL), normal oligoclonal bands, normal synthesis rate and positivity for anti-MOG-IgG antibody. Borrelia IgM antibodies was positive in serum but Borrelia-PCR was negative in serum and CSF. High dose intravenous methylprednisolone induced clinical improvement.

Conclusions:: In our patient the SARS-CoV-2 vaccine may have triggered an autoimmune reaction involving the CNS with the production of MOG-IgG antibody, in a patient with genetic susceptibility and transient vaccine-induced immunosuppression. The clinical and strumental follow-up will be necessary to discriminate between a post-vaccination disease or a MOGAD.

References
Biomarkers Related to the Intrathecal Humoral Immune Response as Laboratory Tools for Multiple Sclerosis Diagnosis

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Background and Aims:: In cerebrospinal fluid (CSF) of multiple sclerosis (MS) patients, the intrathecal synthesis (IS) of affinity-maturated IgG class antibodies secreted by transmigrated B cells, is considered as a hallmark of the disease. It is classically revealed by CSF isofocusing test (detection of IgG Oligoclonal bands (OCB) in CSF, considered as “the gold standard”), Total IgG Index and/or Reiber diagram. Our aim is to analyse the comparative performance of different CSF testing techniques for MS diagnosis.

Methods:: In our study, serum and CSF samples (n=1220) from 610 patients with suspicion of MS diagnosis were analyzed. IgG index was calculated and interpreted using Reiber diagram. IgG-OCB were analyzed by isofocusing test.

Results:: Patients were divided into « MS » (n =192) and « non MS » (n =418) groups according to their clinical and radiological criteria. Regarding MS patients, the mean value of IgG index (1.43) was significantly higher than non-MS group (0.69). Reiber diagram interpretation concluded to an intrathecal synthesis of IgG in 61 % of MS cases and a blood-brain barrier dysfunction in 16 % of cases. CSF isofocusing test revealed an OCB positivity in 87.5 % of MS cases. The specificity of OCB detection test for MS diagnosis was 78%, with a Negative Predictive Value of 93%.

Conclusions:: In routine practice, CSF isofocusing test appears as the most sensitive tool for MS diagnosis with a very high NPV. Quantitative tests (index, Reiberdiagram) are useful to provide faster results and to inform about the brain barrier status.
Background and Aims:: The concomitant presence of atrophy and microstructural abnormalities in multiple sclerosis (MS), as a result of the disease underlying physiopathology, is well documented. Nevertheless, the interplay between atrophy, iron and myelin changes remains elusive. Here we characterized their topography and their contribution to cognitive and motor disability.

Methods:: We analyzed volumetry, relaxometry and susceptibility in 117 MS patients, through voxel-based morphometry and voxel-based quantification analyses on longitudinal relaxation rate (R1) and susceptibility maps in grey matter (GM) and white matter (WM). Voxel-wise between-group differences and correlations between MR metrics and clinical parameters (global disability, cognitive and motor performance) were assessed.

Results:: While R1 decrease was extensive across GM and WM regions in MS patients, susceptibility showed substantially more limited modifications. Atrophy mainly involved deep GM, posterior and infratentorial regions. In several WM tracts R1 and susceptibility were both reduced. Cortex and deep showed a R1 reduction, associated with decreased susceptibility in the thalamus and small clusters of increased susceptibility in the caudate nucleus and cortical areas. Motor disability was associated with GM atrophy and susceptibility values in the cingulum and corona radiata, while cognition was associated with GM atrophy and focal demyelination.

Conclusions:: While demyelination is the prevalent microstructural abnormality in MS, atrophy and modifications of tissue susceptibility seem to have higher clinical relevance, with the former being an indirect marker of neurodegeneration and the latter possibly reflecting oligodendrocyte damage and subsequent reduction of the tissue repair capability.
Background and Aims:: Myelin oligodendrocyte glycoprotein antibodies (MOG-IgG) have been recently reevaluated as a biomarker of acquired demyelinating syndromes (ADS) of the central nervous system (CNS). Here, we describe the clinical and neuroimaging features, and the long-term outcome of children with ADS of the CNS associated with MOG-IgG.

Methods:: All patients underwent brain and spinal cord magnetic resonance imaging (MRI), lumbar puncture for cerebrospinal fluid (CSF) analysis and MOG-IgG and aquaporin-4 IgG (AQP4-IgG) testing.

Results:: Forty-eight pediatric patients were recruited. MOG-IgG were detected in 11/48 (25%) patients with the following clinical presentations: encephalomyelitis (EM), 8/11 (73%); optic neuritis (ON), 2/11 (18%); transverse myelitis (TM), 1/11 (9%). Patients negative for MOG-IgG were diagnosed with Multiple Sclerosis (MS) (n=15), EM (n=7), ON (n=7), neuromyelitis optica spectrum disorders (NMOSD) (n=5), TM (n=2) and encephalitis (n=1). MOG-IgG positive patients were younger at disease onset and they more frequently experienced encephalopathy and epileptic seizures compared with negative patients. EM and inflammatory lesions involving optic nerves on MRI imaging were more frequent in MOG-IgG positive patients. None of the patients with MOG-IgG became persistently seronegative during the follow-up, although a decrease in MOG-IgG titer was observed. Patients with MOG-IgG showed a good response to therapy and only two patients presented relapses during follow-up.

Conclusions:: This study supports the distinction of MOG autoimmune oligodendrocytopathy as a unique disease entity, with clinical features different from those of MS and AQP4-IgG-positive NMOSD.
**Background and Aims:** Syringomyelia (syrinx) is a chronic, progressive, and degenerative disorder of the medulla spinalis. The formation of syrinx can occur as a complication of various disease processes. Multiple sclerosis (MS) is a chronic disease with extensive clinical manifestations that presents as a multifocal area with the destruction of myelin from the CNS. The purpose of this case report is to present the clinical characteristics and MR imaging results of syringomyelia in a patient with multiple sclerosis.

**Methods:** The information is obtained through the patient’s history and medical record.

**Results:** A 20-year-old female patient with 2-year history of secondary progressive MS and bilateral blindness complained that both limbs are weak and cannot be moved progressively. Neurological examination revealed UMN-type inferior paraparesis, normal proprioception and sensory protopathic, and bilateral optic nerve neuropathy. Head MRI with contrast shows MS in the right juxtacortical parietal lobe and left posterior horn of the periventricle lateral area; spinal MRI with contrast shows MS of the spinal cord at C3-C4, C6, T2-T3, T3-T4 and syrinx formation is identified in the central canalis as high as C7 to T10.

**Conclusions:** Patients with a history of MS with demyelinating plaque in the spinal cord can progress and increase their risk of developing spinal syrinx formation.
FINGOLIMOD IN PEDIATRIC MULTIPLE SCLEROSIS: SIX CASE REPORTS

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Background and Aims:: Treatment for pediatric-onset multiple sclerosis (POMS) currently reflects treatment for adult-onset MS, despite some differences in its clinical course. First-choice treatment of POMS generally consists of interferon β-1a or glatiramer acetate, with therapies such as natalizumab or fingolimod reserved for second-choice treatment. In cases of severe disease, both fingolimod and natalizumab can be considered first-choice therapy.

Methods:: This paper presents six case histories of patients with POMS and highlights the different uses of fingolimod within the POMS treatment algorithm.

Results:: Two cases are examples of escalation therapy, both in females aged 16 to 17 years, with fingolimod administering as second choice following disease progression. The other four cases are an example of using fingolimod as first-choice therapy.

Conclusions:: In all six cases, over a period of approximately 1 year after the initiation of fingolimod treatment, there was no further disease progression and no adverse events were recorded.
BILOBALIDE ALLEVIATES CPZ-INDUCED DEMYELINATION VIA SUPPRESSING THE POLERIZATION OF A1 ASTROCYTES

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Background and Aims:: A1 astrocyte exerts neurotoxic effects and is a key factor of failure in nerve repair and myelin regeneration. Bilobalide (BB) is one of the active monomer component of Ginkgo biloba extract, which alleviates the demyelination in Cuprizone (CPZ) model and reduces the secretion of inflammatory cytokines by astrocyte. Our aim was to explore possible mechanisms of BB targeting astrocyte.

Methods:: Primary astrocyte was induced with LPS to establish In vitro inflammatory model, which was divided into normal group, LPS group and LPS+BB group. CPZ model was established in vivo and divided into normal group, CPZ group and CPZ+BB group. From the fourth weekend, CPZ+BB group received injection of BB (400mg/kg/day). The normal and CPZ groups were injected with saline in the same way. The expression of C3d was detected by immunofluorescence and PCR, and the secretions of IL-6, oxidative indexes (GSH-Px, RNS, and MDA) and BDNF, CNTF were detected by ELISA.

Results:: BB inhibited the polarization of A1 astrocyte, reduced the levels of GSH-Px, RNS and MDA, downregulated the secretion of IL-6, and promoted the release of BDNF and CNTF.

Conclusions:: BB can alleviate demyelination by reducing the release of oxidative product and inflammatory factors, and promoting the secretion of neurotrophic factors, which is related to the suppression of A1 polerization. (NNSF of China 81473577, Open Projects of The Key Laboratory of The Ministry of Education 2019004 and Leading Team of Medical Science and Technology, Shanxi Province 2020TD05, China Postdoctoral Science Foundation 2020M680912, Ma and Xiao are corresponding authors)
PATH FEEL SMART INSOLES ARE A RELIABLE TOOL TO ESTIMATE GAIT PARAMETERS FOR MONITORING MULTIPLE SCLEROSIS PATIENTS PROGRESSION.

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Background and Aims:: Multiple sclerosis (MS) patients often exhibit impaired gait related to neurological disability. Light wearable sensors are an opportunity for gait analysis to identify, quantify and monitor gait changes in MS. Path Feel is a smart insole that estimates gait parameters using IMU and pressure sensors. Still, to be used in clinical conditions gait parameters must be reliable. The goal of this study was to investigate the reliability of this smart insole in healthy participants and the minimum detectable changes (MDCs) to describe if the insole is able to detect changes in MS patients.

Methods:: Six healthy participants (30 ± 3 years) participated in two experimental sessions separated by 5 ± 2 days. Participants walked in a 12 [m] walkway three times at their self-selected speed. Cadence, stride length, cycle duration, gait velocity and swing, were compared between sessions using the intraclass correlation coefficient (ICC-2,1) and Bland Altman (BA) plots analysis.

Results:: In total 658 steps were analyzed. Gait parameters showed an ICC > 0.75. BA showed no systematic bias between sessions in any parameter and Limits of Agreements (LoA) are narrow compared to the mean (LoA < 10% mean). Small MDCs were found in all parameters (normalized to mean values ranged from 2–12%).

Conclusions:: Reliability indicated the excellent performance of measuring gait parameters. MDCs are comparable to changes of gait in MS patients. Hence, Path Feel can be a useful tool to monitor MS progression and has the potential to support target-oriented rehabilitative management of MS patients.
THE INFLUENCE OF BIOLOGICAL SEX ON COGNITIVE PERFORMANCE IN PEOPLE WITH MULTIPLE SCLEROSIS

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Background and Aims:: Studies exploring the influence of sex on cognitive performance in people with Multiple Sclerosis (pwMS) are inconsistent and they did not evaluate the interaction effect between sex and clinical/sociodemographic variables (Donaldson et al., 2019; Savettieri et al., 2004). The aim of the study was to evaluate sex differences on cognitive performance and to explore possible interaction effect between sex and clinical/sociodemographic variables.

Methods:: 407 (147 males, 260 females) pwMS according to the latest McDonald criteria were recruited in the study. They underwent a neurological (EDSS) and neuropsychological evaluation (BRB-N). MANOVA and univariate analyses were performed to evaluate main effect of sex on cognitive performance and its interaction with disease duration, physical disability and education. Correction for multiple comparison was performed with Benjamini-Hochberg procedure.

Results:: The main effect of sex was significant on PASAT 3 scores (males>females, F₁,₄₀₆= 11.795, p = 0.001), PASAT 2” (males>females, F₁,₄₀₆=8.883, p = 0.003), SRT-D (females>males, F₁,₄₀₆=5.565, p= 0.019) and WLG (females>males, F₁,₄₀₆=12.697, p < 0.001). Moreover, the sex*education interaction was significant (high education females>low education females) on SPART scores (F₁,₄₀₆=11.486, p = 0.001), SDMT (F₁,₄₀₆=14.486, p < 0.001), SPART-D (F₁,₄₀₆= 6.106, p = 0.014), and STROOP (F₁,₄₀₆= 11.502, p = 0.001).

Conclusions:: The results revealed that biological sex has an impact on long-term verbal memory, attention, processing speed and verbal fluency. Moreover, educational attainment (a proxy of cognitive reserve) seems to have a protective effect only on females on spatial memory, processing speed and inhibitory control.
A CASE OF DELAYED POST-HYPOXIC LEUKOENCEPHALOPATHY FOLLOWING OPIOID INTOXICATION

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Background and Aims:: Delayed post-hypoxic leukoencephalopathy (DPHL) is a rare demyelinating syndrome characterized by cognitive and motor decline. It typically presents with a biphasic course after prolonged cerebral hypo-oxygenation.

Methods:: A 55 years old woman arrived at the emergency department due to a seizure-like episode, after presenting in the previous days a progressive cognitive-motor slowing. The brain CT and blood tests were normal. A month before, she was admitted to another hospital because of respiratory failure following a suicide attempt by medication overdose; she completely recovered in two weeks. After hospitalization in our department, the patient quickly became completely uncontactable and catatonic. The following tests were performed: blood test including screening for autoimmune/paraneoplastic, trombophilic and infective disease, EEG, brain MRI with gadolinium and spectroscopy.

Results:: The neurological examination showed akinetic mutism and catatonia with diffuse limb rigidity and fixed postures. Blood tests were negative; EEG demonstrated a global slowing of the activity. The brain MRI showed a symmetric T2, FLAIR and DWI hyperintensity of the white matter, confluent in the frontal regions. The findings were suggestive of an intramyelinic edema. Control MRI performed after 2 weeks, evidenced a progression of the demyelinating lesions in T2, FLAIR and DWI; spectroscopy demonstrated a decrease of creatine and NAA with an increase of lactate.

Conclusions:: The course of the patient's symptoms, her medical history of recent coma after drug intoxication and the EEG, MRI and spectroscopy findings, as well as the normal or non significant results of other tests for encephalopathies, were strongly supportive for a diagnosis of DPHL.
END OF DOSE INTERVAL (EDI) SYMPTOMS IN PATIENTS UNDERGOING TREATMENT WITH NATALIZUMAB

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Background and Aims:: Many patients treated with Natalizumab experience End of Dose Interval (EDI) symptoms towards the end of the administration cycle. During the pandemic, due to the unknown effects of SARS-CoV-2 infection on patients undergoing treatment with Natalizumab (NTZ), we decided to shift patients on NTZ from a Standard Interval Dosing (SID of 4 weeks) to an Extended Interval Dosing (EID of 5-6 weeks). Our main objective was to study the prevalence and incidence of EDI symptoms in our MS center, along with its efficacy and safety.

Methods:: We reviewed 102 patients in our MS center treated with natalizumab for at least 12 months using EID. When tolerated/possible, patients were shifted from a SID of 4 weeks to an EID of 5-6 weeks. Patients were asked to report any worsening of their symptoms during the administration cycle, fatigue was assessed right before the administration of NTZ, with surveys and Fatigue Severity Scale (FSS).

Results:: Among the 102 patients, 41(40.19%) reported end of dose interval (EDI) symptoms, and the most common one was fatigue. Among those 41 patients: 26(63%) had a Relapsing Remitting (RR) course while 15(37%) had a Secondary Progressive (SP) course. Of note, 15(36.58%) patients reported a new onset of fatigue where none was present before the EID. Our data suggest that with EID efficacy is still preserved since only 6 patients showed new lesions on follow-up-MRI and with little clinical significance.

Conclusions:: Our study shows that when EID was adopted, fatigue was higher in the RR course group, with efficacy still preserved.
THE RELATIONSHIP BETWEEN DEPRESSION AND COGNITION IN MULTIPLE SCLEROSIS: A META-ANALYSIS

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Background and Aims:: Studies on the relationship between depression and cognition in people with Multiple Sclerosis (pwMS) are inconsistent (Arnett, 2005; Baumstarck-Barrau et al., 2011). The aim of the present meta-analysis was to evaluate the possible association between depressive symptomatology and cognitive performance on several cognitive domains in pwMS.

Methods:: The literature search on three electronic databases yielded 5402 studies (4333 after the duplicates removal). 29 studies compared depressive symptomatology (assessed with specific questionnaires) and cognitive performance (outcomes: global cognition, attention, processing speed, verbal, spatial and working memory, verbal fluency, executive functions). Positive ES were indicative of a negative relationship between depression and cognitive performance. A random-effect meta-analysis was performed and mean weighted effect sizes (ES) were calculated using Hedges’ g, via Prometa3 software. Meta-regression analysis served to explore the potential effect of clinical/sociodemographic variables of samples on outcomes.

Results:: Small ES were found in the meta-analysis exploring the relationship between depression and verbal memory (g=0.25, p=0.001), spatial memory (g=0.26, p<0.001), verbal fluency (g=0.30, p<0.001) and executive functions (g=0.33, p=0.002), whereas medium ES were found in the meta-analysis evaluating the possible relationship between depression and global cognition (g=0.53, p=0.016), attention (g=0.47, p<0.001), processing speed (g=0.50, p<0.001) and working memory (g=0.51, p=0.034). Meta-regression analysis revealed no effect of clinical and socio-demographical variables of primary samples on all outcomes.

Conclusions:: Depressed pwMS may show more difficulties in several aspects of cognition, especially those needed to retain, respond and process information in one’s environment, and to those needed be adequately stimulated in processing the relevant information.
ASSOCIATION BETWEEN SMOKING AND RELAPSE IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS UNDER FINGOLIMOD TREATMENT

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Background and Aims:: In relapsing-remitting multiple sclerosis (RRMS), smoking is a known risk factor of disease development and disability progression. However, little is known about the impact of smoking on the efficacy of fingolimod. Here we studied the relationship between smoking and relapses in patients with RRMS under fingolimod treatment.

Methods:: We retrospectively enrolled patients with RRMS who received fingolimod treatment in our hospital between January 2012 and December 2018. Smoking status during fingolimod treatment and clinical data were collected up to December 2019. We conducted survival analysis for clinical relapse during the observation period between smoker and non-smoker groups.

Results:: The study comprised 73 patients with RRMS under fingolimod treatment and 19 (26.0%) of them were smokers. Proportion of patients who relapsed during the follow-up period was higher in smokers than in non-smokers (36.8 vs 11.1%, p = 0.012). Time from the beginning of fingolimod to the clinical relapse was significantly shorter in smokers than the non-smokers (Log-rank test: p = 0.007; Cox proportional hazard model: hazard ratio 4.25 [95% CI 1.36–13.30], p = 0.013). Multivariate survival analysis also showed smoking was an independent risk factor of clinical relapse even after adjusting for sex, age at onset, disease duration, and number of relapses within two years before fingolimod treatment (hazard ratio 5.81 [95% CI 1.57–21.51], p = 0.009)

Conclusions:: Smoking remained a risk factor of disease activity in RRMS patients under fingolimod. Patients with RRMS should be advised to stop smoking even after initiation of high-efficacy drugs.
OUTCOME OF RITUXIMAB THERAPY IN REFRACTORY NEUROMYELITIS OPTICA

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Background and Aims:: BACKGROUND AND AIMS: Neuromyelitis optica (NMO) is a severe autoimmune disease targeting optic nerves and spinal cord. The monoclonal anti-CD20 B cell antibody Rituximab is a treatment option in refractory NMO. The prevalence of NMO in South India is around 2.6/lakh population. This study was conducted to evaluate the outcome of Rituximab over 12 months in refractory NMO.

Methods:: 23 patients of refractory NMO treated with Rituximab who attended the demyelination clinic from January 2017 were studied. Refractory NMO were cases of NMO with at least one relapse on immunosuppressive therapy. A fixed treatment scheme of total four doses of weekly Rituximab at 375mg/m2 and the same repeated every six months, or earlier based on CD19 levels, was given for refractory NMO. The mean annualized relapse rate (ARR) and the median Expanded disability status scale (EDSS) were analysed before treatment and after one year on Rituximab.

Results:: After a mean follow up of 13 months, we observed a significant reduction of median Annualized relapse rate from 2.9 to 0.14 and of the median EDSS score from 5.2 to 3.3. Two patients had relapse while on Rituximab, which was due to inadequate follow up doses of Rituximab. No serious side effects were noted in study group.

Conclusions:: The therapy with Rituximab, with proper follow-up, was found to significantly reduce the frequency of relapses, with subsequent stabilization or improvement in disability.
Patients with multiple sclerosis have poor quality of sleep and frequently suffer sleep related disorders.

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Background and Aims:: Multiple sclerosis (MS) causes physical as well as psychosocial disability in young adults. Various sleep disorders have been reported in patients with multiple sclerosis (pwMS). We determined the frequency of various sleep disorders in pwMS and correlated those with the quality of sleep.

Methods:: IRB approved study at King Abdulaziz Medical City, MNGHA, Riyadh, KSA. Various validated questionnaire were used to assess sleep disorders and quality of sleep.

Results:: Total of 169 patients were included; 116 (69%) were females. Mean age was 35 +/- 10 years, and mean BMI was 27.6 +/- 16.8 kg/m². Almost half (47%) of the patients were employed, most worked in day-shift (85%). Caffeinated beverages were used by 87%; 16% were smokers. Relapsing remitting MS was the commonest type in 93% patients; 82% were using disease modifying therapy. 18% used sleep related medications. EDSS disability was mild in 64%, moderate in 18%, severe in 18%. Poor quality of sleep was reported by 74% (mean PSQI 7.8 +/- 3.9). Circadian rhythm disorders were seen in 22%, psychiatric disorders in 18%, and parasomnias in 14%. 4% had sleep apnea. Psychiatric disorders (p=0.05) and movement disorders (p=0.05) were more frequently seen in women. Insomnia (p=0.03), circadian rhythm disorders (p=0.013) and psychiatric disorders (p=0.002) were associated with poor sleep quality. BMI, neck circumference, type of MS and current treatment did not affect the frequency of sleep disorders or quality of sleep.

Conclusions:: Sleep disorders were common in multiple sclerosis and most patients had poor quality of sleep. Women with multiple sclerosis may be more prone to sleep disorders.
Background and Aims: In the search for an MS diagnostic / prognostic biomarker, circulating microRNAs (miRs) have been in the spotlight. In the context of MS pathophysiological mechanism, several inflammatory miRs have been described as potential diagnostic tools but their prognostic usefulness is yet to be determined. We sought to quantify miR-26a and miR-145, serum levels in MS patients and analyse its diagnostic performance in different groups according to clinical features (MS course and disease activity).

Methods: MiR-26a and miR-145 serum levels were quantified in 90 patients with definitive MS diagnosis accordingly to 2017 McDonald’s Criteria (49F, 6 with Progressive MS, 15 in flare, 29% HLA-DRB1*15 positive, Expanded Disability Status Scale (EDSS) = 2.4 ± 2.1, Multiple Sclerosis Severity Score (MSSS) = 2.8 ± 2.7 Age Related MSSS (ARMSSS) = 3.6 ± 2.6). Twenty-four individuals without autoimmune and neurological pathologies were included in the control group.

Results: MS patients and control individuals had similar miR-26a and miR-145 circulating levels. Also, both miRs were not influenced by clinical form or relapses, nor by HLA-DRB1*15 presence. Noteworthy, miR-26a serum levels were inversely correlated with clinical outcome with lower levels associated with higher MSSS (ρ = -0.370, p = 0.002) and ARMS scores (ρ = -0.288, p = 0.017).

Conclusions: MiR-26a modulates TH17 cells differentiation and phenotype. An imbalance between anti and pro-inflammatory mechanisms could affect MS progression. Our preliminary results suggest that miR-26a could have a role on MS prognosis. Financial support: BIEM
Background and Aims:: There are several approaches to measuring education, such as measures of the time spent in education or the years of education associated with a legally recognized degree/diploma (Connelly et al., 2016). Since raw scores of several neuropsychological tests are corrected for educational attainment, the aim of the present study was to evaluate if different types of measures of education could be associated to possible differences in evaluating the cognitive performance of people with Multiple Sclerosis (pwMS).

Methods:: 412 (63.6% women) pwMS according to the latest McDonald criteria were consecutively recruited in the study. Rao’s BRB-N was administered. Education was calculated in two different ways: a) completed years of education (effective education, EE); b) years associated to a legally recognized degree/diploma (formal education, FE). Corrected and z-scores of BRB-N were calculated on the basis of the two educational approaches to allocate participants in cognitively preserved or impaired groups. Percentages and chi-square test were employed as appropriate.

Results:: Out of 412 pwMS, 91 showed a different number of years of education according to the two approaches. Among the 91 pwMS, 60.4% and 49.5% of pwMS were classified as cognitively impaired according to the EE and FE approaches, respectively. In all tests of BRB-N the significance testing for crosstabulation was significant (p<.001).

Conclusions:: The results revealed that the EE or FE approaches can have an impact on whether considering a pwMS as cognitively preserved or impaired. We suggest that, in future studies, the approach to measuring education should be made explicit.
FLUOXETINE SUPPRESSES TH17-CELLS FUNCTION VIA 5-HT2B-RECEPTOR IN MULTIPLE SCLEROSIS

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Background and Aims:: Fluoxetine is a selective serotonin reuptake inhibitor, which also has an immunomodulatory effect. This study aimed to clarify the influence of fluoxetine on Th17-cells, which plays a crucial role in MS pathogenesis.

Methods:: Thirty MS patients and twenty controls were examined. To assess the effect of fluoxetine on Th17-cells, CD4⁺ T-cells were cultured in the presence of fluoxetine and stimulated with anti-CD3/anti-CD28-antibodies. To study the involvement of 5-HT2b-receptor in fluoxetine-mediated immunomodulation, CD4⁺ T-cells were pre-incubated with antagonists of or agonist of 5-HT2b-receptor, whereafter fluoxetine and anti-CD3/anti-CD28-antibodies were added to the cultures. To assess the direct effect of 5-HT2b-receptor activation on cytokine production, some samples of CD4⁺ T-cells were preincubated with a specific agonist of 5-HT2b-receptor and stimulated as described above. The levels of IL-17, IFN-γ, and GM-CSF in culture supernatants were assessed by ELISA.

Results:: Fluoxetine suppressed IL-17, IFN-γ, and GM-CSF production by stimulated CD4⁺ T-cells in both groups. Blockade of 5-HT2b-receptors decreased the inhibitory effect of fluoxetine on cytokine production in MS patients. Finally, 5-HT2b-receptor activation inhibits IL-17, IFN-γ, and GM-CSF production in both groups.

Conclusions:: These data suggest an anti-inflammatory role for fluoxetine in MS, which could be mediated by the activation of 5-HT2b-receptors. The study was supported by the Russian Foundation for Basic Research grant 18-315-00436.
ALEXITHYMIA IN PATIENTS WITH MULTIPLE SCLEROSIS

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Background and Aims:: To study the prevalence of alexithymia in patients with multiple sclerosis (MS) and to determine the factors related to it.

Methods:: We conducted a cross-sectional, descriptive and analytical study, which took place in the neurology department, at the Habib Bourguiba University Hospital in Sfax. It involved MS patients in remission phase (Mc Donald criteria 2017). Data collection was done using a form exploring sociodemographic, clinical and radiological data. We used the Toronto Alexithymia Scale (TAS-20) and the Expanded Disability Status Scale (EDSS).

Results:: Our study included 93 patients followed for MS. The mean age of our patients was 36.59 ± 10.69 years with a sex ratio (M/F) of 0.45. The participants were married in 57% of cases. The total number of relapses ranged from 1 to 30, with a median of 5. The EDSS score ranged from 0 to 8, with a median of 3.5. A temporal lesion on brain imaging was found in 29% of cases. Alexithymia was found in 54 MS patients (58.1%). It was more frequent in unmarried (single and divorced) patients (p = 0.028). Among clinical and radiological factors, the number of relapses and the EDSS score were higher (p = 0.035 and p = 0.000, respectively) and temporal lesion on brain imaging was more frequent in alexithymic patients (p = 0.045).

Conclusions:: Our study shows that alexithymia affects more than half of the patients followed for MS. Therefore, we propose to develop training programmes for neurologists to detect and manage alexithymic patients at an early stage.
INFLAMMATORY OPTIC NEUROPATHY FOLLOWING SARS-COV-2 MRNA VACCINE: DESCRIPTION OF TWO CASES

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Background and Aims:: A wide range of immune mediated inflammatory events have been temporally associated with vaccinations, and usually appear within weeks after the immunization, although more rarely the delay is longer. Among inflammatory events, optic neuritis is known to be the most common isolated inflammatory syndrome of the central nervous system (CNS) following vaccinations. It has still to be clarified whether optic neuritis will remain an isolated episode or it may represent the first clinical manifestation of a chronic autoimmune disease.

Methods:: Description of clinical history, examination, neuroimaging and treatment of two patients with optic neuritis closely following SARS-CoV-2 mRNA vaccination.

Results:: Two patients aged 48 and 31 years presented with acute optic neuritis a few days after SARS-CoV-2 mRNA vaccination (Fig. 1). The first patient had a typical presentation of unilateral retrobulbar optic neuritis and was treated with intravenous methylprednisolone with partial recovery. Magnetic resonance imaging (MRI) was unremarkable (Fig. 2). The second patient had a transient loss of vision after exposure to high temperature (Uhthoff’s phenomenon) followed by persistent monocular dyschromatopsia and central scotoma.
Conclusions: The two cases we report might represent a rare adverse reaction to SARS-CoV-2 mRNA vaccination. Given the low risk of inflammatory CNS disease following vaccinations and the risk of onset or relapse of CNS demyelination after infections, vaccination benefits outweigh risks. The relationship between mRNA vaccination and later development of CNS demyelinating diseases has still to be ascertained. Clinical and radiological follow up of patients will help clarify this controversial association.
BALANCE DISORDERS IN MULTIPLE SCLEROSIS: THE USE OF POSTURAL TEST IN FUNCTIONAL CLINICAL ASSESSMENT

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Background and Aims:: Multiple sclerosis (MS) is a demyelinating disease of the central nervous system (CNS). A high prevalence of balance disorders has been reported in persons with MS (PwMS), even in the early stages and with minimal disability. Posturography is the current gold standard for balance assessment. Aim of this study was to analyse instability in a cohort of PwMS through postural tests and static posturography and to investigate their correlation with the Extended Disability Status Scale (EDSS) score.

Methods:: We performed a retrospective analysis on 72 PwMS prospectively recruited from 1 May 2015 to 31 October 2019. An in-house standardized postural test and conventional static posturography were performed in every patient. Posturographic data were processed using the Equilibrium software. We used Spearman's rank correlations to relate disability and clinical data obtained from postural tests.

Results:: 48/72 PwMS (66.6%) were female. Mean age was 46.8 (11.6) years, median EDSS 3.5 (IQR 2.5-4.5). The majority (81%) of stabilometric tests were altered. Patients with higher EDSS showed the worst performances. Postural tests, including asymmetric bipodal load, demonstrated high sensitivity but moderate specificity in capturing postural instability when compared to stabilometric measures.
Conclusions: Balance disorders in PwMS still represent a clinical and therapeutic challenge. This study proposes a novel postural test as a useful, non-invasive, quick-and-easy-to-administer screening clinical tool in the diagnosis and follow-up of postural instability in MS. Early detection of balance impairment, especially in patients with low disability, is critical to devise the best rehabilitation strategy to delay functional disability.
BIPOLAR DISORDER IN PATIENTS WITH MULTIPLE SCLEROSIS

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Background and Aims:: To study the prevalence of BD in patients followed for MS and to determine the factors related to it.
Methods:: This was a cross-sectional, descriptive and analytical study, which took place in the neurology department at the Habib Bourguiba University Hospital in Sfax. It focused on MS patients in remission phase (Mc Donald criteria 2017). The questionnaire included sociodemographic, clinical and therapeutic data and two psychometric tools: the Mood Disorder Questionnaire (MDQ) and the Expanded Disability Status Scale (EDSS).
Results:: Our study included 93 patients. The mean age was 36.59 ± 10.69 years, with a sex ratio (M/F) of 0.45. The socio-economic level was high in 47.3% of cases. The patients presented a relapsing-remitting form in 94.6% of the cases. Of the neurological functions affected according to the EDSS, cerebellar function was affected in 33.5% of cases. The total dose of corticosteroids prescribed during relapses ranged from 0 to 100 g, with a median of 15 g. At the time of the study, 79 patients (84.9%) were being treated with disease-modifying therapy for MS: first-line therapy (27.8%) and second-line therapy (72.2%). According to the MDQ, 13 MS patients had BD. The clinical factors associated with BD were the presence of cerebellar function impairment (p = 0.011). Furthermore, no correlation was found between BD and socio-demographic factors or therapeutic factors.
Conclusions:: Our study confirmed the frequency of BD in MS, independent of sociodemographic and therapeutic factors. This link could be secondary to biological, immuno-inflammatory and genetic factors, according to the literature.
EVALUATION OF SUICIDAL IDEATION IN MULTIPLE SCLEROSIS PATIENTS

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Background and Aims:: The aims of our work were to assess suicidal ideation in patients with multiple sclerosis (MS) and to determine the factors associated with it.

Methods:: Our study, descriptive and analytical, took place in the neurology department of the Habib Bourguiba University Hospital in Sfax. It focused on patients with MS in remission (Mc Donald criteria 2017). A pre-established form was used to collect sociodemographic, clinical and radiological data. We also used the Beck Suicide Scale (BSS) and the Hospital Anxiety and Depression Scale (HADS).

Results:: Our study included 93 patients followed for MS. The socio-economic level was high in 47.3% of cases. The duration of MS ranged from 1 to 276 months (median = 72 months). Spinal cord injury and brain atrophy were found on imaging in 71% and 15.1% of cases, respectively. At the time of the study, ten patients (10.8%) reported suicidal ideation. The BSS score ranged from 0 to 21 (median = 0). The BSS score was associated with low to moderate socioeconomic status (p = 0.021) and the presence of spinal cord injury (p = 0.045) and brain atrophy on imaging (p = 0.015). The duration of the disease was also correlated with the suicidal ideation score (p = 0.022). This score was higher in depressed patients (p = 0.000).

Conclusions:: Several psychosocial, clinical and radiological factors could explain the occurrence of suicidal ideation in MS patients. Early detection of suicidal ideation is important in this vulnerable population, especially in the presence of depressive symptoms.
FACTORS ASSOCIATED WITH ANXIETY IN PATIENTS WITH MULTIPLE SCLEROSIS

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\textsuperscript{1}CHU Hedi Chaker hospital Sfax Tunisia, Psychiatry, Sfax, Tunisia, \textsuperscript{2}CHU habib bourguiba Sfax, Neurology, sfax, Tunisia, \textsuperscript{3}Universal Hospital Habib Bourguiba, Neurology, Sfax, Tunisia, SFAX, Tunisia, \textsuperscript{4}Universal Hospital Habib Bourguiba, Neurology, SFAX, Tunisia

**Background and Aims::** To study the prevalence of anxiety in patients with MS and to determine the factors related to it.

**Methods::** This is a cross-sectional, descriptive and analytical study in the neurology department at the CHU Habib Bourguiba in Sfax, among MS patients in remission phase (Mc Donald criteria 2017). The questionnaire included sociodemographic and clinical data and two measurement tools: the Hospital Anxiety and Depression Scale (HADS) and the Expanded Disability Status Scale (EDSS).

**Results::** The 93 patients included in the study had a mean age of 36.59 ± 10.69 years and a sex ratio (M/F) of 0.45. The participants were married in 57% of cases. Eighteen patients (19.4%) smoked, with a daily number of cigarettes between 4 and 25 (median = 12.5). The duration of the disease ranged from 1 to 276 months (median = 72 months). The EDSS score ranged from 0 to 8 (median = 3.5). MS patients had anxiety in 38.7% of cases. Factors correlated with anxiety were: being unmarried (single or divorced) (p = 0.028), high number of cigarettes consumed per day (p = 0.046) and high EDSS score (p = 0.01). We did not find an association between anxiety and gender, nor did we find an association with the duration of the disease.

**Conclusions::** Anxiety is a frequent psychiatric comorbidity in our MS patients, according to the literature. It influences daily functioning by decreasing quality of life, which implies special attention to patients with personal and clinical risk factors to detect anxiety early and treat it in time.
COMORBIDITY IN PEOPLE WITH MULTIPLE SCLEROSIS. A CROSS-SECTIONAL STUDY IN TWO ITALIAN AREAS

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Background and Aims:: The reported prevalence of comorbidities in people with multiple sclerosis (pwMS) varies widely depending on specific comorbid conditions, population evaluated and socio-demographic factors. Our aim is to estimate the prevalence of major comorbidities and to analyze demographic factors related to presence of comorbidity in pwMS.

Methods:: Comorbidity in pwMS was assessed in the period 2012-2017 using a specific algorithm currently used for monitoring prevalence of chronic diseases by Italian Local Health Authorities. The data refer to two study areas of Northern Italy (Pavia, PV and Genoa, GE provinces) where the MS person were identified through a validated administrative MS case definition. Logistic regression models were used to evaluate the risk of having at least a comorbidity considering age class, sex, and study area.

Results:: The MS cases identified were 2984. The 59.5% of pwMS had at least one comorbidity (50.5% GE and 78.6% PV, p<0.001), 64.5% were females (p>0.05) and MS GE population was slightly older (GE median=50 vs PV median=49 years, p=0.005). The most prevalent comorbidities were: depression (32.8%), cancer (29.2%), hypertension (18.0%), heart disease (7.8%), hyperlipidaemia (7.3%) and cerebrovascular diseases (7.1%). Presence of comorbidities were significantly less likely among males (OR 0.8, p=0.008) and more likely in PV area (OR=4.57, p<0.001) and among older age groups (ORs from 1.31 to 9.58 considering the different age classes, p<0.001).

Conclusions:: Our study shows the importance of considering population-based characteristics when evaluating comorbidities in MS as prevalence may vary based on age, sex and residence geographic area.
THE LINK BETWEEN MULTIPLE SCLEROSIS AND DEPRESSION

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2CHU habib bourguiba Sfax, Neurology, sfax, Tunisia,
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Background and Aims:: To study the prevalence of depression in patients with MS and to determine the factors related to it.

Methods:: Our study, descriptive and analytical, focused on patients followed for MS at the neurology department, Habib Bourguiba University Hospital in Sfax. In addition to collecting sociodemographic, clinical and radiological data, we used the Hospital Anxiety and Depression Scale (HADS) and the Expanded Disability Status Scale (EDSS).

Results:: The 93 patients included in the study had a low to medium socio-economic level in 52.7% of cases. The duration of MS ranged from 1 to 276 months (median = 72 months). The EDSS score ranged from 0 to 8 (median = 3.5). Urinary function was affected in 37.6% of cases. On imaging, frontal and spinal cord lesions were found in 47.3% and 71.1% of cases respectively. MS patients had depression in 26.9% of cases. Patients with a low to medium socio-economic level were more depressed (p = 0.006). The clinical factors of MS associated with depression were: the duration of the disease (p = 0.031), the severity of disability (p = 0.000) and the impairment of urinary function (p = 0.027). As for radiological factors, the presence of a frontal lesion and a spinal cord lesion on MRI was associated with depression (p = 0.001 and p = 0.028, respectively).

Conclusions:: The results of our study showed that depression was common in MS patients. It would be wise to develop a multidisciplinary approach with collaboration between neurologists and psychiatrists to improve the management of this psychiatric comorbidity.
ADMINISTRATIVE DATA TO ESTIMATE THE BURDEN OF MAJOR COMORBIDITIES IN MULTIPLE SCLEROSIS. A CROSS-SECTIONAL STUDY IN TWO ITALIAN AREAS

Maria Cristina Monti1, Giulia Mallucci2, Michela Ponzio3, Paola Borrelli1,4, Eleonora Rigoni2, Sara Fusco2, Dabiela Amicizia2,5, Giampaolo Brichetto3, Maria Francesca Piazza5, Pietro Perotti6, Santino Silva7, F Ansaldi8, Mario Battaglia9, Cristina Montomoli1, Roberto Bergamaschi10

1University of Pavia, Department Of Public Health, Pavia, Italy, 2IRCCS Mondino Foundation, Multiple Sclerosis Research Centre, Pavia, Italy, 3Italian Multiple Sclerosis Foundation, Scientific Research Area, Genova, Italy, 4University “G. d’Annunzio” Chieti-Pescara, Department Of Medical, Oral And Biotechnological Sciences, Laboratory Of Biostatistics, Chieti, Italy, 5Liguria Health Authority, A.l.i.s.a, Genova, Italy, 6Health Protection Agency, Ats, Pavia, Italy, 7Health Protection Agency, Pavia, Pavia, Italy, 8University of Genoa, Department Of Health Sciences, Genova, Italy, 9University of Siena, Department Of Life Sciences, Siena, Italy, 10IRCCS Fondazione Mondino, Centro Sclerosi Multipla, Pavia, Italy

Background and Aims:: Although comorbidity is important in Multiple Sclerosis (MS), there are few validated methods for its assessment. Our aim is to estimate the burden of major comorbidities in people with MS (pwMS) in two Northern Italy study areas (Pavia, PV and Genoa, GE), using routinely collected healthcare data.

Methods:: We estimated prevalence of comorbid conditions in pwMS in the period 2012-2017 using a specific algorithm currently used for monitoring prevalence of chronic diseases by Italian Local Health Authorities (BDA system). Direct healthcare costs were defined by regional and governmental contracts; the aggregated healthcare expenditure was compared between pwMS with/without comorbidities and by sex, age class and area of study.

Results:: The MS cases identified were 2984, 2035 in GE and 949 in PV and 59.5% of pwMS had at least one comorbidity. The mean direct healthcare costs of MS were substantially higher for individuals with comorbidity (36,135 € vs 25,796 €, p<0.001), showing 40% of additive costs.

Conclusions:: Our study provides evidence of the burden of comorbidities in MS. Comorbidity is common in MS and produce additive costs. The use of administrative data for tracking the MS comorbidity could help to improve knowledge’ gaps. Moreover, when an additivity situation is involved, preventive policies could lead to monetary savings.
Background and Aims:: The pathogenesis of multiple sclerosis (MS) is multifactorial, being controversial whether there is a relationship between this disease and cancer. A recent study reported an increased risk of primary central nervous system cancer (PCNSC) but a decreased overall risk of other cancer (OC) in MS patients.

Methods::

<table>
<thead>
<tr>
<th>Feature</th>
<th>Valor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age* (SD)</td>
<td>38.2 (SD 9.37)</td>
</tr>
<tr>
<td>Gender (%)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>6 (35.9%)</td>
</tr>
<tr>
<td>Women</td>
<td>11 (64, 1%)</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>8 (47%)</td>
</tr>
<tr>
<td>Comorbidities (%)</td>
<td>5 (29.4%)</td>
</tr>
<tr>
<td>First grade relative(s) with MS (%)</td>
<td>6 (35.9%)</td>
</tr>
<tr>
<td>MS after Cancer (%)</td>
<td>6 (35.2%)</td>
</tr>
<tr>
<td>PCNSC</td>
<td>5 (83.3%)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (18.7%)</td>
</tr>
<tr>
<td>Cancer after MS (%)</td>
<td></td>
</tr>
<tr>
<td>PCNSC</td>
<td>2 (18.1%)</td>
</tr>
<tr>
<td>Other</td>
<td>9 (80.2%)</td>
</tr>
</tbody>
</table>

Table 1. Demographic characteristics of patients with diagnosis of MS and cancer. PCNSC: primary central nervous system cancer. OC: other cancer. *Mean / median. SD: standard deviation. IQ: interquartile range 25-75.

Methods: We performed an observational, analytic, retrospective, case-control study at National Medical Center “Siglo XXI”, in Mexico City. All patients whom got cancer diagnosis after MS diagnosis criteria were include. Our list includes type of cancer, immunomodulatory (IM) drugs used and gender.

Results::
11 patients were included, while only 2 (18.1%) got PCNSC. Incidence in women was higher than in men [9 (81.8%) versus 2 (18.1%); P < .05]. Breast cancer was present in four patients (36.3%), while 2 was treated with glatiramer acetate, and 2 with fingolimod. Other IM used in patients with cancer were interferon and mitoxantrone, with no statistically significant evidence of relationship between IM and an specific type of cancer. The Odds Ratio (OR) for getting cancer diagnosis after MS being woman was 20.25 with 95% confident interval of 1.24-16.25 (p value 0.0028).

**Conclusions:** Being woman is by itself a risk factor for the development of cancer after MS treatment and breast cancer was the most frequent type. We have not reported an increased risk of brain cancer after long-term exposure to IM. No data support an increase in cancer risk among MS patients treated with IM.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer after MS</td>
<td>3.361</td>
<td>0.88-3.816</td>
<td>0.086</td>
</tr>
<tr>
<td>Cancer after MS being woman</td>
<td>20.25</td>
<td>1.24-16.25</td>
<td>0.0028</td>
</tr>
<tr>
<td>Cancer after MS age at diagnosis &gt; 35 y</td>
<td>1.44</td>
<td>0.51-2.78</td>
<td>0.66</td>
</tr>
<tr>
<td>Cancer after MS PCNSC</td>
<td>0.049</td>
<td>0.061-0.80</td>
<td>0.0028</td>
</tr>
<tr>
<td>Cancer after MS OC</td>
<td>20.25</td>
<td>1.24-16.25</td>
<td>0.0028</td>
</tr>
<tr>
<td>Breast</td>
<td>0.64</td>
<td>0.313-2.03</td>
<td>0.637</td>
</tr>
<tr>
<td>Skin</td>
<td>0.494</td>
<td>0.061-0.80</td>
<td>0.0028</td>
</tr>
<tr>
<td>Seminoma</td>
<td>0.0156</td>
<td>0.019-0.08</td>
<td>0.0009</td>
</tr>
<tr>
<td>Teratoma</td>
<td>0.0156</td>
<td>0.019-0.08</td>
<td>0.0009</td>
</tr>
<tr>
<td>Endometrium</td>
<td>0.0156</td>
<td>0.019-0.08</td>
<td>0.0009</td>
</tr>
<tr>
<td>OC after MS exposure to Interferon</td>
<td>0.816</td>
<td>0.080-1.018</td>
<td>0.018</td>
</tr>
<tr>
<td>OC after MS exposure to Acetate glatiramer</td>
<td>0.64</td>
<td>0.31-2.038</td>
<td>0.637</td>
</tr>
<tr>
<td>OC after MS exposure to Mitoxantrone</td>
<td>0.816</td>
<td>0.080-1.018</td>
<td>0.018</td>
</tr>
<tr>
<td>OC after MS exposure to Fingolimod</td>
<td>0.25</td>
<td>0.178-1.40</td>
<td>0.157</td>
</tr>
</tbody>
</table>

RESULTS OF LONG-TERM FOLLOW-UP AFTER HIGH-DOSE IMMUNOSUPPRESSIVE THERAPY AND AUTOTRANSPLANTATION OF HEMATOPOIETIC STEM CELLS (ATHSC) IN PATIENTS WITH A SECONDARY PROGRESSIVE MULTIPLE SCLEROSIS (SPMS).

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Background and Aims:: Most authors evaluate ATHSC as an effective treatment method for remitting and rapidly progressing MS. The question of the feasibility of using ATHSC in the SPMS remains poorly understood.
To evaluate the long-term results of ATHSC based on clinical and radiological data in patients with SPMS.

Methods:: We analyzed data from 14 MS patients aged 29 to 47 years, who were observed in the center for more than 5 years with a good clinical response to transplantation. Pretransplantation conditioning was performed according to the standard protocol: BEAM+ALG.

Results:: The duration of the disease before transplantation is from 9.0+ 5.1years, EDSS - from 4.5 to 6.5 points. The duration of follow-up after ATHSC is from 60 to 148 months. After ATHSC, there was an improvement in the condition in 6 patients with a decrease in EDSS by 0.5 points. The condition was stabilized in 8 patients with no signs of activity according to MRI data. After two years, the condition was stabilized in 11 patients, 3 patients showed deterioration with further accumulation of disability. The five-year progression-free survival rate was 35 %.

Conclusions:: SPMS is of a clinical and immunological heterogeneous nature, where inflammatory activity may persist. The best results after ATHSC were observed with the duration of the disease up to 10 years, the level of EDSS no more than 6.5 points, a low index of disease progression, as well as episodes of exacerbation disease in the anamnesis.
INVESTIGATION OF FATIGUE AND ANXIETY IN PATIENTS WITH MULTIPLE SCLEROSIS DURING COVID-19

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Background and Aims: People with MS (PwMS) have a higher burden of neuropsychiatric comorbidities and are known to undertake maladaptive coping strategies in stress conditions. The aim of this study was to understand the effects of the COVID-19 epidemic process and epidemic measures on anxiety and fatigue in MS patients.

Methods: The study was designed as a prospective, cross-sectional survey study. The early stage of COVID-19 outbreak (ESO) data were collected on January, 2020 and the peak stage of COVID-19 outbreak (PSO) data were collected on April, 2020. Individuals who were being followed with a diagnosis of RRMS or SPMS and an EDSS score of ≤4.0 were included in the study. Participants' depression states were evaluated with the Beck Anxiety Inventory (BAI) and fatigue states were evaluated with the fatigue effect scale (FIS).

Results: The study included 61 PwMS (Female: 83.60%). The average age of the participants was 29.4±7.24. BAS levels of the patients showed a significant increase in PSO compared to ESO (p<0.01). In FSI measurements, the cognitive subscale scores and the total FIS score were significantly at PSO compared to ESO (p<0.05 for all), whereas no significant difference was found with regard to the physical and social subscale scores (p>0.05).

Conclusions: The results of this study show that the anxiety levels and fatigue of MS patients continue to increase together during the COVID-19 process. As the COVID-19 outbreak continues to widen, our findings will provide vital advice for the development of a psychological support strategy and priority areas in areas affected by the outbreak.
ANCESTRALITY AND FAMILIAL RECURRENCE RATES OF MULTIPLE SCLEROSIS IN BRAZIL

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Background and Aims:: Familial multiple sclerosis is defined as multiple sclerosis cases occurring in at least two family members, and there is no data on the recurrence risk of familial multiple sclerosis in the Brazilian population, which is characterized by a high frequency of afrodescendants as a result of the miscegenation occurred between European settlers and African slaves. Objective: To estimate the multiple sclerosis recurrence risk in patient families in Rio de Janeiro (RJ) and investigate the relationship with Caucasian and African ancestry.

Methods:: A cross-sectional study was conducted in Rio de Janeiro (Brazil), with 197 patients followed by a RJ specialized outpatient clinic. Recurrence risks were calculated by relative multiple sclerosis patient categories through age-adjusted Crude recurrence risks.

Results:: Familial multiple sclerosis frequency (7.10%) was identified in the RJ study population. The risk of Age-adjusted recurrence (ARR) was high among grandparents, at 2.72 (95% CI 2.16 - 3.28). Sibling ARR was calculated as 1.41 (95% CI 1.22 - 2.08), and Caucasian ancestry conferred a risk of 1.96. Concerning the parent relationship, ARR was of 1.57 (95% CI 1.36 - 1.78) and increased to 1.76 (95% CI 1.41 - 2.11) in the presence of a European ancestor. Among uncles/aunts, a significant increase from 1.42 (95% CI 1.01 - 1.83) to 2.91 (95% CI 2.28 - 3.54) risk in individuals with Caucasian ancestry was observed, and to 2.65 (95% CI 2.02 - 3.27) in individuals with African ancestry.

Conclusions:: A higher risk among individuals with Caucasian ancestry was observed compared to Afro descendant ancestry.
THE PREVALENCE OF COVID-19 INFECTION IN PATIENTS WITH MULTIPLE SCLEROSIS (MS): A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims:: There prevalence of COVID-19 is different in studies conducted in different countries. The aim of this systematic review and meta-analysis is to estimate pooled prevalence of COVID-19 in MS patients.

Methods:: Two independent researchers independently searched PubMed, Scopus, EMBASE, Web of Science, and google scholar along with gray literature up to 23th of October 2020. The search strategy included the MeSH and text words as (((coronavirus OR Wuhan coronavirus OR novel coronavirus OR coronavirus disease OR COVID-19 OR 2019 novel coronavirus infection OR 2019-nCoV OR severe acute respiratory syndrome coronavirus 2 OR SARS-CoV-2) AND (Multiple Sclerosis OR Sclerosis, Multiple) OR Sclerosis, Disseminated) OR Disseminated Sclerosis) OR MS (Multiple Sclerosis) OR Multiple Sclerosis, Acute Fulminating).

Results:: We found 1460 articles by literature search, after deleting duplicates 1023 remained. Twelve articles remained for meta-analysis. Totally 16577 patients were evaluated and total number of possible/confirmed cases was 570. Mean age ranged from 35-54 years. Totally 4 patients died. The pooled prevalence of COVID-19 in MS patients was 4% (95% CI: 2%-5%) (I^2=95%, P <0.001). The pooled prevalence of hospitalization in infected cases was 15% (95% CI: 8%-23%) (I^2=92%, P<0.001). The pooled prevalence of death in infected cases was 0% (I^2=0, P=0.9).

Conclusions:: Hospitalization rate is higher among MS patients based on COVID-19 while the pooled infection rate estimated as 4%.
PREVALENCE OF COVID-19 INFECTION IN PATIENTS WITH NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOSD): A SYSTEMATIC REVIEW AND META-ANALYSIS.

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Background and Aims:: The novel coronavirus disease (COVID-19) is in pandemic stage and there are concerns about patients with autoimmune diseases.

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Background and Aims:: The novel coronavirus disease (COVID-19) is in pandemic stage and there are concerns about patients with autoimmune diseases.
Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory disease of the central nervous system (CNS) which predisposes cases to increased risk of infection based on immunosuppressive treatments.
Conclusions:

The pooled estimate of COVID-19 infection in NMSD patients was 2% (95% CI: 0.7%-7.0%) (I2=80.6%, p<0.001).

Conclusions: Prevalence of COVID-19 infection is rare in NMSD patients.

Methods:

We systematically searched PubMed, Scopus, EMBASE, Web of Science, and Google Scholar and also gray literature up to the included studies. The search strategy included the MeSH and text words as ((coronavirus OR Wuhan coronavirus OR novel coronavirus OR coronavirus disease OR COVID-19 OR 2019 novel coronavirus infection OR 2019 CoV) AND (Neuromyelitis optica spectrum disorder OR NMOSD OR Devic syndrome OR Neuromyelitis optica spectrum disorder)).

STMATA (Version 13.0; Stata Corp LP, College Station, TX, USA) was used for data analysis. Inconsistency (I2) was calculated for heterogeneity evaluation.

Results:

The literature revealed 54 articles. Totally, 3458 patients with NMOSD were evaluated. The pooled estimate of COVID-19 infection in NMOSD patients was 2% (95% CI: 0.7%-7.0%) (I2=80.6%, p<0.001).

Conclusions: Prevalence of COVID-19 infection is rare in NMOSD patients.
PSYCHOMETRIC PROPERTIES OF CROATIAN VERSION OF THE MULTIPLE SCLEROSIS INTIMACY AND SEXUALITY QUESTIONNAIRE-15

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Background and Aims:: Multiple sclerosis (MS) is a chronic demyelinating inflammatory progressive disease of the central nervous system that results in a wide range of clinical manifestations and has a great impact on patient quality of life. The aim of this study was to determine the psychometric properties of Croatian version of the multiple sclerosis intimacy and sexuality questionnaire-15 (MSISQ-15).

Methods:: A cross cultural adaptation of the MSISQ-15 into Croatian and a psychometric analysis of the translated version of the MSISQ-15 was carried out in MS patients. The MSISQ-15 includes three subscales: primary - MS related neurologic changes that may directly affect sexual feelings and/or sexual response; secondary - MS related physical changes that affect the sexual response indirectly; and tertiary - referred to the psychosocial and cultural aspects of MS that affect sexuality. The data was descriptively analysed and Cronbach’s alpha assessed internal consistency. Pearson’s correlation was performed on the MSISQ-15 total scale and subscale scores. The level of significance was set to p<0.05.

Results:: Eighty-two MS patients were assessed (mean age 42.6±11.9 years, 62.2% females). The means score for the MSISQ-15 total scale, primary, secondary and tertiary subscales were 33.35±13.00, 12.01±5.38, 11.31±4.47 and 10.04±5.37, respectively. Cronbach’s alpha for the MSISQ-15 total scale was 0.93 (range for subscales: 0.84-0.92). The total MSISQ-15 scale significantly correlated with all subscale scores (Pearson correlation range: 0.77-0.91).

Conclusions:: The Croatian version of the MSISQ-15 can be a valid and reliable instrument for multiple sclerosis intimacy and sexuality problems in Croatian-speaking MS patients.
DIFFERENCES IN MS CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS IN ASHKENAZI AND NON ASHKENAZI JEWISH PATIENTS IN ISRAEL – A RETROSPECTIVE SINGLE CENTER STUDY

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Background and Aims:: Background: The prevalence and severity of Multiple Sclerosis (MS) are diverse across different ethnicities, with a tendency to a more severe phenotype in Non-Caucasian populations. Objective: Our objective was to evaluate the differences in disease phenotype between Ashkenazi and Non-Ashkenazi Jewish patients in Israel.

Methods:: We conducted a retrospective cohort study based on clinical charts. Subjects were assigned to Ashkenazi or Non-Ashkenazi groups according to self-reported ancestry and disease severity was assessed using the expanded disability status (EDSS), MS severity score (MSSS), progression index (PI) and MRI metrics.

Results:: We identified 330 Ashkenazi and 207 Non-Ashkenazi patients. Non-Ashkenazi patients were younger at evaluation (43.0 years vs. 49.4 years) and at disease onset (32.7 years vs. 35.7), with a lower proportion of females (62.3% vs. 73.3%). MSSS was higher in Non-Ashkenazi patients (3.29 vs. 2.91) when adjusted to covariates using propensity score analysis and in patients with relapsing remitting MS (RRMS) when analyzed separately (2.47 vs. 1.90).

Conclusions:: Non-Ashkenazi Jewish patients scored higher in disease severity scores, were diagnosed at an earlier age and demonstrated a narrower sex gap as compared to Ashkenazi Jewish patients. These findings might contribute to prognosis evaluation and motivate further epidemiological and genetic investigation.
CLINICAL AND PARACLINICAL FINDINGS IN A CASE SERIES OF MOGAD: EXPLORING THE PRESENCE OF PERIVENULAR BRAIN WHITE MATTER LESIONS

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Background and Aims:: Clinical and histopathological manifestations of the MOG associated disease (MOGAD) may overlap with those of multiple sclerosis (MS) and of NMO spectrum disorders (NMOSD), and histopathological findings consistent with MS pattern II lesions have been reported. To further explore clinical and radiological phenotype of MOGAD, evaluating for the first time the presence of perivenular brain white matter lesions (PVL).

Methods:: We retrospectively reviewed the records of a single Neurology clinic for MOGAD cases, analyzing clinical and paraclinical findings.

Results:: In the patients included (n= 11), median age 27 (range 19-52), the most frequent clinical manifestation at onset was optic neuritis (73%), bilateral in 62% of the cases. Intrathecal oligoclonal IgG production in CSF was never observed. Over a median follow-up of 16 months, 36% of patient experienced a clinical relapse. At last follow-up, 36% of the patients met the 2015 NMOSD diagnostic criteria and none of them fulfilled the 2017 McDonald criteria for MS. At baseline MRI, 6 out of the 10 patients with an available scan had at least one brain lesion, that resulted located in a “MS typical” site in 4/10 cases. Corticospinal tract lesions were present in 2/10 cases. Several PVLs were observed in the case showing evaluable lesions.

Conclusions:: Our case series displays several clinical and paraclinical specific features of MOGAD, despite a few brain MRI findings overlapped with MS. The observation PVLs in one case warrants further studies investigating the potential clinical value of the central vein sign for the differential diagnosis between MS and MOGAD.
Background and Aims:: Peripheral nervous system in form of nerve or a radicle can also be involved in NMOSD and MOGAD. Kim et al postulated that CNS-PNS transition zone i.e the radicles are main target as they contain AQP4.

Methods:: This was a prospective observational study done for 15 months. Inclusion criteria: Patients with age >13y who satisfy IPND NMOSD diagnostic criteria or MOGAD. Exclusion criteria: Patient who have past history of neuropathy or any disease which can cause peripheral nerve involvement. Eg:- T2DM & Vasculitis. All patients underwent sensory and motor nerve conduction studies including F wave.

Results:: 95 patients were included in study. Mean age was 33.99 ± 13.8 years. Male: Female =1:3. Isolated optic neuritis (ON) was the presentation in 57(60%), isolated myelitis in 25 (32.6%), myelitis with ON in 12(12.6%), brainstem syndrome in 1(1.1%), diencephalic syndrome in 1(1.1%) and area postrema syndrome in 6(6.3%) 30% patients had neuropathic symptoms. AQP4 antibody was positive in 37% patients, Anti MOG was positive in 15% and both were negative in 52%. NCS was abnormal in 41 (43.2%). Among which demyelination pattern was seen in 16(39%) and axonal pattern was seen in 25(61%). Abnormal NCS was found the least in patients of age 12-20 years (p=0.00).
Conclusions: We hypothesize that presence of Aquaporin-4 at extracranial site would lead to complement mediated inflammation and axonal nerve damage. Our study showed significant association of peripheral demyelination in dual antibody negative patients. So, we think there could be association of other antibodies in these disorders which would cause demyelination in the peripheral nervous system.
GUILLAIN BARRÉ SYNDROME DURING THE ZIKA PANDEMIC FROM 2016 TO 2019 IN VERACRUZ, MEXICO.

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Background and Aims:: During the Zika pandemic in southeastern Mexico, there was an increase in Guillain Barré cases initially attributable to viral neurotropism demonstrated in other latitudes

Methods:: We conducted a descriptive, retrospective, and longitudinal study in Veracruz, Mexico, where follow-up of cases of Guillain Barre Syndrome (GBS) occurred during 2016 to 2019. The central point of the study is to look for the etiological association of GBS with the presence of acute zika infection. Secondly, other known neurotropic agents, both viral and bacterial were searched. The diagnosis techniques used were PCR-RT (blood and urine) and IgM/IgG for Zika; serum PCR-RT and IgM/IgG for Dengue and Chikungunya; IgM/IgG for TORCH; PCR-RT in CSF for Herpes and Enterovirus; serological panel of Hepatitis B and C; PCR-RT in rectal swab for Campylobacter.

Results:: A cohort of 40 patients has been formed over 4 years of study, of which only 2 cases were identified by PCR-RT in urine; others were identified such as: Dengue, Chikungunya, Enterovirus, Herpes and Hepatitis B; however, the identification of Campylobacter was even more remarkable, also highlighting that only four patients had diarrhea. Regarding the treatment, 38 patients received IVIG, 1 patient received plasmapheresis and 1 patient received both. The prognosis was good in 35 patients (basal Hugues from 4–5 to 2), 5 had poor functional prognosis and died.
Conclusions: During the Zika pandemic in southeast Mexico, the main agent of Guillain Barré syndrome cases was Campylobacter, the incidence of Zika and other viruses with neurotropic potential was low, so campylobacter should always be considered.
FREQUENCY AND EFFECT OF DONEPEZIL ON COGNITIVE DYSFUNCTION IN PATIENTS WITH MS OF UZBEK NATIONALITY

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Background and Aims:: About half of all MS patients experience problems with memory and other cognitive functions. Because there have been limited trials of donepezil in MS and the results have been mixed, the current evidence of the efficacy of donepezil on cognitive function in people with MS is unclear. Donepezil is a cholinesterase inhibitor. It is thought to work by inhibiting an enzyme which breaks down acetylcholine, which is a chemical in the central nervous system that acts as a neurotransmitter - carrying messages from nerve to nerve. Therefore, donepezil increases levels of acetylcholine.  
Methods:: This study included 16 (100%) admitted Uzbek patients with a diagnosis of MS who applied to the local Family Hospital during the period 2017-2020. In 7 (43.75%) patients, cognitive impairment was observed as a decreased memory and thinking. 3 of them (18.75%), by their consent, took the drug Alzancer (Donepezil) in a dose of 10 mg, 1 tab daily for 120 days.  
Results:: Of the 3 (18.75%) patients taking donepezil, only 2 (12.5%) noted a slight improvement in memory 90-100 days after the start of the drug. 1 (6.25%) patient, comparing the periods before and after taking the drug, did not indicate any (positive or negative) changes in memory and thinking.  
Conclusions:: The number of patients with cognitive impairment was 7 (43.75%). Taking donepezil 10 mg, 1 tab daily for 120 days did not have a significant positive effect on the cognitive impairment of patients with MS in the local family clinic.
MULTIPLE SCLEROSIS ENVIRONMENTAL RISK FACTORS AT BEJAIA, AN ALGERIAN STUDY.

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Background and Aims:: Multiple Sclerosis (MS) is an inflammatory and degenerative disease of central nervous system. This condition involves multiple genetic and environmental factors. The aim of our study is to evaluate environmental related risk factors.

Methods:: A cross-sectional study carried out during 2020 at the University Hospital of Bejaia in Algeria. Data were collected using a risk factors questionnaire inspired from the international ENVIMS study.

Results:: We collected 35 cases of MS with an F/M sex ratio of 1.9. Mean age of disease onset was 28±6.62 years. Analysis objectified low vitamin D levels in 51.42% of cases, overall reduced physical activity (82.9%), irregular sun exposure during childhood (35%) and adolescence (71.4%), high body mass index (BMI) values (48.6%), active (25%) and passive smoking habits (54%). We have found significant associations, between high relapses frequency and each of high BMI, vitamin D deficiency and low sun exposure during childhood. On the other hand, low relapses frequency was correlated with regular physical activity and long breastfeeding period. Low initial EDSS was related with normal BMI and infant breastfeeding too.

Conclusions:: Vitamin D deficiency, reduced sun exposure in childhood, smoking and insufficient physical activity during adolescence, appear to be risk factors of developing MS in adulthood.
MORPHO-FUNCTIONAL ALTERATIONS IN AUTOSOMAL-DOMINANT LEUKODYSTROPHY (ADLD): THE INTRIGUING ROLE OF THE ASTROCYTES

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Background and Aims:: Autosomal Dominant Leukodystrophy (ADLD) is a rare and fatal adult-onset neurodegenerative disorder that affects the central nervous system. It is characterized by Lamin B1 (LMNB1) gene duplication or deletion upstream the gene, but the molecular mechanisms responsible for driving the onset and development of this pathology are not clear yet. Considering the pivotal role that glial cells as oligodendrocytes and astrocytes, and Leukemia Inhibitory Factor (LIF)-activated signaling pathways have in the myelination process, this work aims to analyze the specific alterations in different cell populations

Methods:: Specific morpho-functional aspects of ADLD patients' primary cells and engineered cellular models overexpressing Lamin B1 have been analyzed.

Results:: Cells from ADLD patients and astrocytes overexpressing LMNB1 show several nuclear alterations, not present in oligodendrocytes overexpressing LMNB1. Moreover, the accumulation of Lamin B1 in astrocytes induces a reduction in LIF and in LIF-R levels with a consequential decrease in LIF secretion, leading to the downregulation of Jak/Stat3 and PI3K/Akt axes, downstream of LIF/LIF-R in both the cellular models. Administrating exogenous LIF, the toxic effects, induced by LMNB1 accumulation, may be partially reverted with differences between astrocytes and oligodendrocytes. In addition, it was observed that astrocytes are undergoing apoptosis, highlighting that LMNB1 overexpression drastically affects astrocytic function reducing their fundamental support to oligodendrocytes in the myelination process. Finally, it has been shown the activation of proinflammatory mechanisms and increase of reactive oxygen species (ROS) in ADLD patients’ cells.

Conclusions:: Our studies point out, for the first time, that astrocytes may be pivotal in the development of the
disease.
PROSPECTIVE LONG-TERM TOCILIZUMAB RESPONSES IN RELAPSING MYELIN OLIGODENDROCYTE GLYCOPROTEIN IGG-ASSOCIATED DISEASE AND FACTORS ASSOCIATED WITH POST-TOCILIZUMAB RELAPSE-FREEDOM

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Background and Aims:: Tocilizumab (TCZ), an anti-interleukin-6 receptor antibody, shows promise in treating myelin oligodendrocyte glycoprotein-associated neurological disease (MOGAD). However, large prospective studies are lacking, while determinants for post-biologic disease response remain unclear. We prospectively evaluated long-term TCZ-responses in relapsing MOGAD and associated-factors for post-TCZ relapse-freedom.

Methods:: 195 aquaporin-4 antibody-negative adult MOGAD patients with relapses despite ≥3 immunosuppressants (5 highly-specialised neurology-centres) received intravenous TCZ (8mg/kg 4-weekly) for 4years (2017–2021). We characterised pre- and post-TCZ annualised relapse rates (ARR), Expanded Disability Status Scale (EDSS) scores, radiological progression, adverse events (AE), features of those with and without post-TCZ relapses, and elucidated factors for relapse-freedom and odds ratios (OR) by logistic regression.

Results:: Mean age, MOGAD onset-age and disease duration were 47.9, 42.1 and 5.8years, with 566 pre-TCZ clinical demyelinating-episodes (mean 2.9/patient). 63.1% previously used rituximab. Post-TCZ initiation, 21.0% relapsed over 4years (86.1weeks to first relapse). TCZ reduced cumulative ARR (1.81 to 0.11, p<0.0001) and median ARR 18months pre- and post-initiation (2.0 to 0.0, p=0.0009). Previous rituximab-users had lower ARR during TCZ-treatment than rituximab (0.11 vs 0.53, p=0.0007). TCZ mildly-improved EDSS (3.36 to 2.87, p=0.004). 84.6% and 61.0% showed no post-TCZ EDSS or radiological progression. Post-TCZ 4-year survival was 90.8%. 81.0% developed AEs (43.1% infections, 5.1% severe). Post-TCZ relapse-freedom independently-associated with 1 pre-TCZ relapse (OR4.38, p=0.003), pre-TCZ MOGAD duration<2years (OR2.19, p<0.001), onset-age<40 (OR1.83, p=0.001), and no autoimmune comorbidities (OR3.52, p=0.002).

Conclusions:: TCZ reduces MOGAD relapse and disability over 4years. 1 pre-TCZ relapse, pre-TCZ MOGAD duration<2years, onset-age<40 and no autoimmune comorbidities heralded superior responses, identifying those likely to show greater TCZ-response. Efficacy of TCZ-initiation after first relapse warrants further investigation.
EFFICACY OF FINGOLIMOD IN THE 2ND LINE TREATMENT OF ACTIVE RELAPSING-REMITTING MULTIPLE SCLEROSIS: ABOUT A TUNISIAN COHORT OF 50 PATIENTS

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Background and Aims:: Fingolimod (FING) is the first oral immunomodulatory treatment approved for the 2-line disease-modifying treatment of active relapsing-remitting (RR) forms of multiple sclerosis (MS). Observational post-marketing studies are important for clarifying the efficacy and safety of the product in current medical practice. The Aim of our study is to assess the effectiveness of FING in patients with RR-MS followed at the National institution of neurology in Tunis.

Methods:: An observational study on 50 patients with MS, older than 18 years, treated with FING for the first time for a period of ≥ 3 months between 2015 and 2019 and followed up at the National institution of neurology in Tunis.

Results:: FING was initiated at a mean age of 41.3 years (± 10). The mean duration of progression of MS before the initiation of FING was 11.42 years. The mean annualized relapse rate (APR), under the first-line treatments was 1.11, with a significant decrease in APR before and after treatment with FING (from 1.11 to 0.38 under FING, relative risk reduction of 65.76% (p <10^{-3}). 42.6% of patients became free from relapses on FING after an average duration of treatment with FING of 32.1 months. 26 patients (57%) did not present with progression of disability under FING. In multivariate analysis, the duration of the progression of MS at FING introduction was the predictive factor of progression of MS with FING (OR= 2.24, p= 0.018).

Conclusions:: Earlier introduction of FING as soon as the failure of the first-line treatment could improve its effectiveness and the control of relapses.
IMPACT OF THE SARS-COV 2 PANDEMIC ON PATIENTS WITH MULTIPLE SCEROSIS : A TUNISIAN STUDY

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Background and Aims:: In the context of SARS-COV2 pandemic, patients with multiple sclerosis (MS) constitute a vulnerable population due to the assumptions made about the risk of severe infection and the limitation of access to health care. We aim to study the sanitary and therapeutic impact of the SARS-cov2 outbreak on patients with MS.

Methods:: We conducted a cross-sectional study including patients followed for MS. The study period was divided into two: pre-pandemic (October to March 2020) and pandemic (March to June 2020). The diagnosis of MS was selected according to the criteria of Mc Donald (2017). Added to collecting data from medical files, we carried out a telephone questionnaire regarding therapeutic compliance, aggravation or installation of new neurological symptoms.

Results:: Seventy-two patients (mean age =32.6 years, mean EDSS =3.8) were included. During confinement, 16 patients stopped their basic treatment because of the non-authorization of inter urban travel and the fear of contamination by SARS-cov2 upon arrival at hospitals. Compared to the pre-pandemic period during which 24 patients (50% discontinuing treatment) had a relapse, 20 patients (16 without basic treatment) reported worsening of neurological symptoms and the use of corticosteroid therapy in consulting (50 %) and hospitalized patients. Multivariate statistical analysis showed that non compliance and relapses’ frequency did not differ before and during pandemic and that the occurrence of relapses is correlated with non-adherence to therapy.

Conclusions:: It is necessary to make informed decisions about MS treatment management in order to minimize the health impact of this pandemic.
STATUS EPILEPTICUS INAUGURATING MULTIPLE SCLEROSIS: “ONE TRAIN HIDES ANOTHER”: A CASE REPORT

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Background and Aims: The prevalence of epilepsy is 4.5 to 6 times higher in patients with multiple sclerosis (MS) than in the general population. Only few cases have proven a direct causal relationship with MS. Is this just a frequent combination or symptomatic attacks of MS? Are these attacks the result of an acute flare-up of the disease?

Methods: We report the case of a patient followed in our neurology department in Mahdia for MS, inaugurated by status epilepticus.

Results: A young mother of 26 years, presented a status of epilepticus, made of focal motor tonicoclonic right hemi-bodily seizures with secondary bilateralisation. The neurological examination outside of the seizures was without abnormality, except for the presence of sharp tendon reflexes in the 4 limbs without Babinski's signs. Cerebral-medullary MRI revealed multiple demyelinating lesions of the white matter, with the presence in particular of nodular juxta-cortical lesions and a small left upper frontal cortical lesion. Note the absence of spinal cord injuries and signs of activity. The diagnosis of MS was retained in view of young age, female sex, spatial dissemination on brain MRI, the presence of oligoclonal bands in the CSF, the absence of red flags. The patient received a 5-day bolus of solumedrol and put on Levet 500 mg 1cp * 2/d and interferonB. We note the recurrence of seizures after 4 months due to non-adherence to antiepileptic drug. A control MRI showed the increased lesion burden.

Conclusions: Epilepsy may be the only symptom of MS. An exhaustive etiological assessment is obligatory. “One train hides another”
MULTIPLE SCLEROSIS INCIDENCE UPDATE IN PROVINCE OF FERRARA, NORTHERN ITALY, DURING COVID19 ERA.

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Background and Aims:: Previous descriptive surveys on multiple sclerosis (MS) in the province of Ferrara carried out by our own epidemiological research group in the previous decades, pointed out that this area was not at low-medium risk for MS. We aim to confirm the above assumption and to update MS frequency estimates in this area

Methods:: We used a complete enumeration approach by reviewing all the possible sources of case collection available in Ferrara for 2016 through 2020. We included all patients with definite and probable MS according to the Poser criteria

Results:: The incidence cases were 84, 22 men and 62 women. The mean incidence for the period 2016-2020 was 4.86 per 100,000 (95 % CI, 1.66-4.01), 6.91 for women and 2.65 for men. The adjusted incidence to the European population was 6.01 per 100,000/year. The incidence temporal trend in 1965-2020 is shown in Figure 1.

Conclusions:: In the province of Ferrara MS appears to occur more frequently than suggested by the geographic-related distribution model. The slowly incremental incidence trend cannot be solely attributed to improvement in diagnostic capability, but – likely - to variation of exposure to exogenous risk factors in genetically predisposed individuals. The incidence rate over the study period remained relatively stable compared what previously observed (1965-2015), and a not significant decrease in 2019 and 2020 (Figure 2) was recorded, likely representing an underestimation in relation to the contingent COVID19 pandemic and the consequent difficulty in accessing health
Background and Aims:: The diagnosis of Neuromyelitis Optica spectrum disorder (NMOSD) can be challenging especially in patients with atypical presentations and unknown serostatus for aquaporin-4 antibodies (AQP4-Ab). We present three cases with different onset variations and relapsing episodes and aims to present and compare the clinical, radiological and evoked potential findings.

Methods:: This is a prospective serial case of three patients. A 20-year-old female presenting with acute myelopathy with a history of optic neuritis and a 26-year-old female presenting with bilateral optic neuritis with a history of myelopathies, both cases shown optic nerve involvement in head MRI. The third case was a 46-year-old female presenting with acute myelopathy and history optic neuritis with a normal MRI finding. They were no distinctive lesion for Multiple sclerosis (MS) in all cases, yet they were treated as MS and results in more frequent episodes of relapse and disabilities. A Visual evoked potential help evaluate the optic nerve involvement in all three cases and the diagnosis was concluded by presence of a lesion that extends three or more adjacent vertebral segments.

Results:: In all three cases, they were treated as NMO with prednisone and azathioprine and there were no relapse for two years follow up.

Conclusions:: It is important for clinicians to distinguish the cause of the clinical picture, and radiological imaging criteria that was beneficial in the establishment of patient’s diagnosis whether is an NMOSD or MS. Because the two diseases have different treatments with different prognoses.
THE IMPORTANCE OF OPTICAL COHERENCE TOMOGRAPHY IN THE DIAGNOSIS OF SUBCLINICAL OPTIC NEURITIS

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Background and Aims:: Optic neuritis (ON) is an inflammatory condition of the optic nerve. ON is often associated with development of demyelinating diseases of the central nervous system (CNS), such as multiple sclerosis (MS) or neuromyelitis optica spectrum disorders (NMOSD). CNS lesions visualized by magnetic resonance imaging (MRI) and finding of oligoclonal bands (OB) in the cerebrospinal fluid (CSF) are used to stratify risk of MS after "first" episode of ON, so-called clinically isolated syndrome (CIS). However, diagnosis of ON in the absence of typical clinical manifestations can be challenging.

Methods:: Here we present 3 cases of changes in the optic nerve and its neuron in the retina over disease course.

Results:: 1) A 34-year old female with history of migraine and hypertension had suspect amaurosis fugax (transient vision loss) in the right eye. This patient developed MS 4 years later. Optical coherence tomography (OCT) showed dynamic changes of the thickness of peripapillary retinal nerve fiber layer (RNFL) and macular ganglion cell-inner plexiform layer (GCIPL) over time. 2) A 29-year old male with spastic hemiparesis and lesions in the brain stem at onset. Six years later he had bilateral subclinical ON identified using OCT. The patient fulfilled diagnosis of antibody-negative NMOSD. 3) A 23-year old female with overweight and headache had bilateral optic disc swelling. With OCT, idiopathic intracranial hypertension (IIH) was excluded. Further investigation showed positive antibody for myelin oligodendrocyte glycoprotein (MOG).

Conclusions:: These three cases illustrate importance of using OCT to facilitate quick, accurate diagnosis of subclinical ON, and thus proper therapy.
APOE GENOTYPE AND COGNITIVE IMPAIRMENT IN MULTIPLE SCLEROSIS; IS THERE A LINK?

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Background and Aims:: Cognitive impairment (CI) is one of the prevalent, but neglected symptoms of multiple sclerosis (MS). Apolipoprotein E (ApoE) is one of the genetic factors associated with human cognition. We investigated the role of the ε4 isoform of ApoE (ApoE4) in CI in MS patients.

Methods:: After obtaining informed consent, adult (18+) mildly disabled (EDSS score<4) relapsing-remitting MS (RRMS) patients, based on 2017 revised MacDonald criteria, were assessed by the approved Persian version of minimal assessment of cognitive function in MS (MACFIMS) battery. After determining the genotype of ApoE, patients were divided into two groups of ApoE4 positive and negative, and the frequency of CI was compared. CI was defined as was at least 1.5 standard deviations below the mean normative value in the Iranian population.

Results:: 71 patients, including 54 ApoE4-positive cases, were participated in this study. There was no significant difference between study groups in demographic factors. At least one impaired test in MACFIMS battery was observed in 64.70% of patients in the ApoE4 positive and 29.62% of the ApoE4 negative group (p<0.01). The rate of overall CI, which was defined as a failure in ≥2 tests, was not different between groups of the study (p=0.75). In a detailed investigation of the components, failure in Paced Auditory Serial Addition Test (p=0.01) was the only difference.

Conclusions:: MS ApoE4 positive patients are susceptible for CI and should be followed up strictly with MS-specific cognitive tests. The existing controversies between the studies, highlight a need for future well-designed studies with larger sample sizes.
Background and Aims:: Distinguishing Vegetative from Minimally Conscious State (VS; MCS) is a challenge due to the difficulty in relating observed behaviors with underlying brain activity. The visual responses in the visual subscale of the Coma Recovery Scale-revised (CRS-r) are informative of the change from VS to MCS; however, few studies explored the functional and structural integrity of the visual system in these patients.

Methods:: Forty-two DoC patients showing visual blink, and twelve showing visual pursuit were enrolled in the study. All of the patients had a diagnosis of VS except for the visual subscale of the CRS-r. For each participant, we collected flash Visual Evoked Potentials (fVEPs), structural Magnetic Resonance Imaging (MRI) of the visual system, and Positron Emission Tomography with 2-deoxy-2-[fluorine-18]fluoro-D-glucose (FDG-PET) variables to explore difference between groups.

Results:: Patients manifesting visual pursuit showed a better fVEPs response, greater integrity at the level of right V1 and optic radiation, and a difference for the cluster localized in the right calcarine cortex and lingual gyrus.

Conclusions:: Despite the role of V1 in conscious visual processing is still controversial, our results highlighted the importance of primary visual areas for conscious visual behaviors. The lateralization of neuroimaging results is supported by the right-hemisphere dominance for top-down modulation in visuospatial processing. The fVEPs results indicated how differences can be detected even by easily applicable exams, as our fVEPs data were not able to detect higher-order visual processing. In concluding, multimodal measures would be adopted as they can help clinicians for diagnostic purposes.
PERSONALLY - EMOTIONAL SPHERE IN PATIENTS WITH MILD TRAUMATIC BRAIN INJURY

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Background and Aims:: One of the earliest and most significant disorders in traumatic brain injury (TBI) is a violation of the emotional and personal sphere. To study the degree of anxiety and depression in patients with mild traumatic brain injury.

Methods:: We examined 83 patients with TBI (42 men and 41 women aged 47.8±9.5 years) and 10 healthy individuals matched by sex and age. To check for anxiety Spielberg-Hanin scale, to check the depression rate - Tsung scales were used.

Results:: We tested the levels of anxiety and depression in patients to assess their personal emotional state. 73 (87.9%) of patients who underwent mild TBI had anxiety with an average of 44±9.7 points on the Spielberg-Hanin scale. This condition was associated with moderate to severe anxiety (31-45 points). All patients had higher personal anxiety rates rather than reactive anxiety, 65.4% and 34.6% accordingly. When patients with BC had light and moderate anxiety levels, patients with TBI and TE had all types of anxiety. When compared the levels of anxiety in patients with mild TBI according to time, there was a critical difference between early and late recovery periods (p<0.05).

Conclusions:: Personally - emotional disorders are not unique to the acute phase of the injury, but may increase levels of depression as a result of impaired serotonin metabolism in the dynamics. It is therefore advisable to assess the levels of anxiety and depression in the dynamics.
INTERRACRANIAL PRESSURE IN ADOLESCENT CHRONIC POST-TRAUMATIC HEADACHE AND ITS TREATMENT

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Background and Aims:: Although chronic post-traumatic headache (CPTH) is a life disturbing disorder for adolescence, it is usually attributed to neurosis or somatoform disorders. We have reported the possibility of increased intracranial pressure (ICP) in adult CPTH (Eur J Med Res 2007; 12: 246-54)). The purpose of this study is to investigate the ICP in adolescent CPTH.

Methods:: We retrospectively investigated ICP measured by lumbar spinal tap in 17 patients less than 20 yo with CPTH for over 3 months. Body mass index (BMI) was also calculated. Causes of trauma, disease period, and characteristic of the headache were also investigated. Data were demonstrated in median (IQR). All patients received epidural saline and oxygen injection (ESOI) (Acta Neurochir Suppl 2013; 118: 293-6).

Results:: Age was 14 years (IQR; 13, 16.5). There were 11 males and 6 females. The ages were 13 yeas (11, 17) and 14 (13.75, 16.25). All patients complained headache with orthostatic nature. ICP was 168 (141.5, 230) and BMI was 19.2 (17.55, 23.6). Disease period was 8 months (4.5, 15). All patients improve by ESOI and 3patients were completely cured.

Conclusions:: Although the headache had orthostatic nature suggesting low ICP, ICP in adolescent CPTH was high that cannot be attributed to obesity. The result of this study indicates the importance of measuring ICP inb adolescent CPTH. Epidural saline and oxygen injection is a promising therapeutic modality.
MODIFIED SPINAL CORD STIMULATION (MSCS) PROMOTED TO AWAKEN THE PATIENTS WITH CHRONIC UNCONSCIOUSNESS

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Background and Aims:: Chronic patients with unconsciousness after brain injury often require long-term monitoring and treatment, which is expensive and usually leads to heavily psychological and economic burden. Our aim was to analyze the applicable value and economic effect of the modified spinal cord stimulation (MSCS) for the treatment of unconsciousness in chronic patients.

Methods:: In this study, we used real-world research methods (Non-randomized concurrent standard control study and historical control study). Sixty chronic patients with unconsciousness from August 2020 to August 2022 in General Hospital of National Medicine and Datong Coalmine were divided into experiment group (n=30) , standard control group (n=20) and historical control group (n=10) . The patients in experimental group were treated with early implementation of MSCS, the patients in standard control group were treated with routine clinical treatment and the patients in historical control group were treated with clinical routine treatment before 2020. We carried out awareness assessment and intuitive-quantitative electrophysiological examinations to evaluate the applicable value of MSCS at four time points: pre-operaton, and 1, 3 and 6 months after surgery.

Results:: The recovery rate and consciousness level of patients in experimental group were significantly higher than those of other two groups with a significantly lower medical cost and shorter length of hospitalization stay.

Conclusions:: MSCS is clinically applicable and economically valuable, which is worth spreading in the treatment of unconsciousness due to chronic illness. (Funding for Key Laboratory of Prevention and Treatment of Neurological Diseases, 2020SYS20, Huang is corresponding author)
NEUROAID USE IN TRAUMATIC BRAIN INJURY (TBI)

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Background and Aims: The ongoing NeuroAiD Safe Treatment (NeST) Registry (ClinicalTrials.gov Identifier NCT02536079) examined NeuroAiD safety and efficacy in a cohort of traumatic brain injury (TBI) subjects from Malaysia. MLC601/MLC901 (NeuroAiD) is a formulation of natural products shown to aid neurological recovery after injury, especially ischemic stroke. Its evidence still remains limited in TBI.

Methods: The online NeST Registry prospectively collected data at baseline and visits (V) 1, 2, and 3, included demographics; medical conditions; clinical assessments of Glasgow Coma Scale (GCS), modified Rankin Scale (mRS), and Short Orientation Memory Concentration Test (SOMCT); compliance; concomitant medications; and adverse events.

Results: This analysis included 23 subjects, of whom 18 had data until V3. Median age was 36 years (range 15-64), with 17% (4) female. Median GCS at baseline was 11 (moderate TBI). Median time from injury to NeuroAiD administration was 20 days (range 7-40). All clinical assessments showed improvement over time. At baseline, only 30%(7) had GCS of 13-15, improving to 83%(15) by V3. For functional independence per mRS, none had mRS 0-1 at baseline, improving to 33%(6) by V3. For cognitive function per SOMCT score, 61%(14) had severe cognitive impairment at baseline, decreasing to only 22% (4) by V3. There were 2 subjects with deterioration of GCS score (only 1- and 2-point decrease) but their level of functional independence per mRS was preserved. No other adverse events were noted.

Conclusions: MLC601/MLC901 is demonstrated to be a safe adjunctive therapy for aiding recovery in TBI. Larger studies should further assess its safe use in enhancing TBI recovery.
REDUCTION IN HYPERMETABOLIC STATE ON MIDAZOLAM STEWARDS ANTICONVULSIVE TREATMENT FOR INTERICTAL PATTERNS IN SEVERE ACUTE BRAIN INJURY: A PILOT MR PERFUSION STUDY.

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Background and Aims:: Small Cohorts have utilized PET and SPECT scans as complementary markers of metabolic activity in status epilepticus in patients with ictal-interictal EEG patterns (IIC). While some rhythmic/periodic discharges mandate termination, other IIC patterns reflect underlying stable brain lesions with no superimposed cerebral injury. We realize that perfusion mapping is not the greatest surrogate; however, it is more readily available. We suggest severe brain injury patients be treated with aggressive anticonvulsive treatment only when they fulfill all the following criteria: 1) altered mental status, 2) IIC EEG patterns, 3) periodic/rhythmic discharges colocalizing with hypermetabolism detected by loco-regional hyperperfusion and 4) significant decrease in hyperperfusion during a midazolam (MDZ) test.

Methods:: A cohort of neuro-ICU patients with criteria 1 and 2 underwent MRI with a repeat run of arterial spin labeling, assessing the response of hyperperfusion foci to brief anticonvulsive therapy with 2mg of MDZ.

Results:: Our pilot study established the frequency of IIC patterns that coincide hyperperfused foci. We are now doing the analysis to quantify the hyperperfusion and how much it decreased during the MDZ test. Outcome measures will include incidence of subsequent seizures, new FLAIR lesions, and degree of neurologic disability.

Conclusions:: Subsequent studies will compare the effect of treating only patients with criteria 1&2, v-s 1-3, vs. 1-4. Our study is limited by the use of perfusion as a surrogate for metabolism, the absence of simultaneous EEG during the imaging study and deficiency in standardized quantification for hyperperfusion during the ictal processes. These are slightly addressed by patient specific analysis and pharmacological challenge.
TAILORED NEUROPHYSIOLOGY: QUANTITATIVE EEG UNCOVERS SUBCLINICAL ISCHEMIA/OLIGEMIA AND REDEFINES PENUMBRA AMENABLE TO BLOOD PRESSURE OPTIMIZATION.

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Background and Aims:: Continuous quantitative EEG (cqEEG) is used in critical care for prognosing coma, or to identify non-convulsive seizures and early injury secondary to ischemia. We report on our expansive utilization of cqEEG in a neuro-ICU for 1) enhanced detection of widespread subclinical ischemia/oligemia, 2) defining oligemia with positive response to mild hemodynamic augmentation (HDA), a.k.a. perfusion optimization-responding syndrome (PORS) and 3) optimization of blood pressure (BP) for penumbral salvage.

Methods:: In ten subarachnoid hemorrhage (SAH) patients, cqEEG was used because of other modalities presaging vasospasm. In 3 other patients, 1 with acute ischemic stroke (AIS) and 2 in vasospasm after SAH, we used cqEEG to ascertain the need for HDA for penumbral salvage. In these 3 patients, PORS was confirmed and cqEEG was continued to assess our induced adjustments in BP.

Results:: Relative alpha variability (RAV), alpha-delta ratio (ADR) and alpha power (AP) by quadrant, hemispheric suppression ratio (HSR), these EEG findings together provide enhanced revelation of subclinical ischemia. PORS was identified by an increase in AP or decrease in HSR. PORS enabled us to recognize those patients who required escalation in HDA. Once started, fine-tuning of BP goals was based on quadrant AP & ADR, allowing for more accurate adjustments, compared to adjustments guided by clinical parameters alone.

Conclusions:: cqEEG is an invaluable modality in identifying the need for “pressing” a patient and in gauging induced hypertension. cqEEG should not be used only in coma but in parallel with clinical examinations in all brain injured patients who are at risk for secondary ischemia.
Background and Aims:: Traumatic brain injury (TBI) is one of the leading causes of death and disability worldwide with an African incidence estimated at around 8 million cases per year. We report this study to describe the socio-demographic, clinical, paraclinical and evolutionary characteristics.

Methods:: This is a descriptive retrospective study lasting one (1) year from March 2020 to February 2021, carried out at the Neurology Unit of the National Reference Teaching Hospital in N’Djamena. Our study included complete records of patients hospitalized for suspected or documented TBI. Sociodemographic, clinical, paraclinical, therapeutic and evolutionary data were collected and analyzed using SPSS 2.0 software.

Results:: Out of 219 files examined, 24 (22 men) had met the selection criteria. The mean age of our patients was 37.5 ± 16.1 years old. The 25 to 34 age group was the most affected with 29.2% of cases. Traders and motorcycle drivers (Clandoman) were the most represented with 25% (n = 6) for each. Road accidents were the most common causes with 79.2% (n = 19). 45.8% of patients had a Glasgow Coma Scale (GCS) ≥13; 29.2% had a GCS between 12 and 9 then 25% had a GCS ≤ 8. Fifteen patients had performed a brain scan. Hemorrhagic or edema-hemorrhagic contusions were found in 53.3% of patients. The mean time to hospitalization was 7.7 ± 4 days. The outcome was favorable in 87.5% (n = 21) of cases, the death rate was 12.5% (n = 3).

Conclusions:: TBI is a major public health problem, especially in low- and middle-income countries.
INTRODUCING THE WCN CONSCIOUSNESS SCALE: A COMPREHENSIVE TOOL TO ASSESS CONSCIOUSNESS IN THE CRITICAL CARE SETTING.

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Background and Aims: Different specialties use different neurologic terminology, scales and flowsheets when it comes to the assessment of unconscious patients in critical care units, and no agreement identifies slight decreases in the degree or content of consciousness. Mild decrements in consciousness without full deterioration can be assessed with a simple clinical examination to assess nuanced domains of consciousness more accurately than AVPU, JCS, GCS, FOUR, RASS, CAM-ICU or NIHSS.

Methods: We systematically reviewed commonly used consciousness scales, and obtained criteria for arousability and alertness from each scoring system. Sensitivity and specificity of GCS, RASS, FOUR and NIHSS item 1 were tested against our proposed compound scale during neuro-ICU rounds.

Results: Scoring alertness before/after stimuli, attention span, processing speed, gauging of the arousing stimulus and quality of the response, period at peak alertness, all carry more value than arousa or attention alone, such as measured by GCS or RASS; respectively. Our combined assessment is considerably more consistent and valuable than degree of orientation (“AOx3”). We noted that trainees from different residencies and neurosciences nurses had more consistent assessments of consciousness. Furthermore, identification of deterioration was earlier. Contrasted to standard charting, our tool is conducive of more accurate terminology, better clinical documentation, and keener inter-professional communication.

Conclusions: The WCN Consciousness Scale better establishes arousability, alertness, and attention. It likely outperforms GCS and RASS. We urge neurologists, neurosurgeons and critical care experts to join forces and establish a sensitive basic scale of consciousness to allow easier communication as well as utilize it in research to readjust trial endpoints.
SMOKING ASSOCIATED WITH INCREASED ODDS OF POST-CONCUSSIVE SYNDROME IN LARGE CROSS-SECTIONAL STUDY

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Background and Aims:: Post-concussion syndrome (PCS) affects 30% of those who suffer a concussion, with symptoms such as memory difficulties and mood changes. The evidence between smoking and PCS in humans is unclear. Some studies correlate smoking with slower neurocognitive recovery whilst others merely demonstrate a higher symptom severity in those who do not recover.

Methods:: A cross-sectional study of 1,563 users of Mindset4Dementia, an application developing screening tests for dementia, was performed. The Rivermead Post-Concussion Symptoms Questionnaire (RPQ) was used to assess PCS symptoms. Lifestyle factors and scores from two modified cognitive tests, the Stroop and Symbol Digit Modality Test, were also collected. Regression models were used to assess the effect of concussions on cognitive tests scores and the correlation of lifestyle factors to RPQ scores.

Results:: 360 individuals had suffered at least one concussion with 318 Individuals completing the RPQ. Individuals with previous concussions performed worse on the Stroop Test (beta = -0.08, p<0.001) with a trend to worse performance on the Symbols Digit Modality Test (beta = -0.04, p = 0.063). Smoking (beta = 0.23, p = 0.001) but not alcohol (beta = -0.05, p =0.2) was strongly associated with an increase in the odds of PCS (OR 3.03, CI 1.44 - 6.42, p = 0.003) as assessed by a cut-off of 16 on the RPQ-13.

Conclusions:: Although the cross-sectional nature of the study makes causation difficult to establish, this study provides preliminary evidence that smoking is associated with the development of PCS.
EFFICACY AND SAFETY OF ANDEXANET ALFA FOR FACTOR XA INHIBITORS USE ASSOCIATED INTRACRANIAL BLEEDING: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims:: Direct oral anticoagulants use has been significantly expanded from atrial fibrillation, deep vein thrombosis and pulmonary embolism to use in cancer patients, and some surgical patients in the last decade. Favored pharmacokinetics and pharmacodynamics, predictable effects, few drug interactions favors oral Factor Xa inhibitors over traditional Vitamin K antagonists. However, fatal bleeding as unfavored event are also reported with its use. In May 2018, FDA approval use of Andexanet Alfa (AA) in patients treated with rivaroxaban and apixaban, in the setting of life-threatening or uncontrolled bleeding. This systematic review and meta-analysis was conducted to analyze the effectiveness and safety profile of AA in bleeding caused by Factor Xa inhibitors to fully appraise the role of AA.

Methods:: PubMed, Pubmed Central, Scopus, Embase and Cochrane library were searched for relevant studies. Covidence was used for screening of literatures based on inclusion and exclusion criteria. RevMan 5.4 was used for quantitative synthesis. Odds ratio (OR) and mean difference (MD) was used to estimate the outcome with a 95% confidence interval (CI).

Results:: 1245 studies were identified after a thorough database search and three studies were included for analysis. Analysis using fixed effect model showed AA resulted in lower odds of mortality compared to 4F-PCC (OR, 0.37; 95% CI, 0.20-0.71) among patients with intracranial hemorrhage. There was no difference in thrombotic events, length of hospital stay, and ICU stay were seen between patients receiving AA and 4F-PCC.

Conclusions:: AA reduced in-hospital mortality in patients who had bleeding due to Factor Xa inhibitors compared to 4F-PCC.
ROLE OF DEXAMETHASONE IN CHRONIC SUBDURAL HEMORRHAGE: A SYSTEMATIC REVIEW AND META-ANALYSIS

Dhan Shrestha1, Pravash Budhathoki2, Yub Sedhai3, Pearlbiga Karki4, Pinky Jha4, Gaurab Mainali4
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Background and Aims:: Chronic Subdural Hematoma is a neurological condition characterized as a hematoma of subdural with a time period greater than 3 weeks that primarily affects elderly. Apart from surgical intervention, pharmacologic and conservative therapies are used. Glucocorticoid especially dexamethasone either alone or in combination with surgery are used in the management of Chronic Subdural Hematoma.

Methods:: PubMed, PubMed Central, Scopus, and Embase were search for relevant articles till December, 2020. Relevant data, including study characteristics, quality, and endpoints were extracted and analysis was done by RevMan 5.4. Handling of data and combining results of the studies were done using OR and random or fixed effect model based on heterogeneities.

Results:: The odds for recurrence of subdural hemorrhage was lowered by 61% in the steroid group (OR, 0.39; 95% CI, 0.19 to 0.79) comparing to control group. There was no significant difference in mortality during study period (OR, 0.66; 95% CI, 0.20 to 2.18), modified Rankins Score (mRS 0-3) (OR, 0.87; 95% CI, 0.31 to 2.40), and mRS 4-6 (OR, 1.15; 95% CI, 0.42 to 3.18) between two groups using the random effect model. However, pooling data from three studies showed 2.7 times higher odds of occurring adverse effects in steroid groups using the fixed effect model (OR, 2.70; 95% CI, 1.71 to 4.28).

Footnotes:
(1) Repeat surgery for recurrence during study period
(2) at 3 months
(3) T=Steroid and Drain + steroid
<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Steroid with SOC</th>
<th>Control</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>------------------</td>
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</tr>
<tr>
<td>2.2.1 Steroid with Surgery vs. Steroid alone</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Kostas F, et al. 2018</td>
<td>1</td>
<td>25</td>
<td>3</td>
</tr>
<tr>
<td>Sun TF, et al. 2005</td>
<td>3</td>
<td>69</td>
<td>1</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>4</td>
<td>94</td>
<td>36</td>
</tr>
<tr>
<td>Total events</td>
<td>4</td>
<td>94</td>
<td>36</td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 1.57; Chisq = 2.09; df = 1 (P = 0.15); I² = 52%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.87 (P = 0.38)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.2.2 Steroid with Surgery vs. surgery alone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kostas F, et al. 2018</td>
<td>1</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>Minh PP, et al. 2020 (DECSA - R)</td>
<td>7</td>
<td>60</td>
<td>13</td>
</tr>
<tr>
<td>Gian Z, et al. 2017</td>
<td>6</td>
<td>75</td>
<td>33</td>
</tr>
<tr>
<td>Sun TF, et al. 2005</td>
<td>3</td>
<td>69</td>
<td>2</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>229</td>
<td>375</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total events</td>
<td>17</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.00; Chisq = 0.43; df = 3 (P = 0.92); I² = 0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 3.00 (P = 0.003)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.2.3 Steroid alone vs surgery alone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kostas F, et al. 2018</td>
<td>3</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Sun TF, et al. 2005</td>
<td>1</td>
<td>26</td>
<td>2</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>36</td>
<td>143</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total events</td>
<td>4</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 4.34; Chisq = 4.92; df = 1 (P = 0.03); I² = 80%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.15 (P = 0.86)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>2.2.4 Steroid vs Placebo/Conservative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hutchinson PJ, et al. 2020 (Des-CSH)</td>
<td>6</td>
<td>341</td>
<td>25</td>
</tr>
<tr>
<td>Sun TF, et al. 2005</td>
<td>1</td>
<td>26</td>
<td>2</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>367</td>
<td>343</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total events</td>
<td>7</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.39; Chisq = 1.34; df = 1 (P = 0.25); I² = 26%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.55 (P = 0.018)</td>
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</tbody>
</table>

Test for sub-group differences: Chisq = 2.04; df = 3 (P = 0.58); I² = 0%.
Conclusions:: Treatment with steroid was associated with lesser recurrence of subdural hematoma. However, there was no benefit of steroid treatment in chronic subdural hematoma compared to non-steroid treatment in terms of mortality, treatment success and increased risk of adverse events.
BLOOD PRESSURE TARGET IN NEUROSURGICAL PATIENTS: HOW HIGH AND HOW LOW SHOULD WE GO?

Stanlies D’Souza
University of Massachusetts Medical School, Neuroanesthesiology, Baystate Medical Center, Springfield, United States of America

**Background and Aims::** The cerebral autoregulation is considered to be dynamic rather than static as it was originally thought. The revised lower limit of cerebral autoregulation, narrower range of autoregulation in neurosurgical patients and data from randomized controlled trials and large retrospective analysis required the revision of blood pressure (BP) targets in neurosurgical patients.

**Methods::** The review of the neuroscience literature from 2010-2020 using PUBMED, EMBASE and the Brain Trauma Foundation (BTF) 2016 guidelines.

**Results::**

<table>
<thead>
<tr>
<th>Neurosurgical Condition</th>
<th>BP target in mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traumatic brain injury (TBI)</td>
<td>Cerebral perfusion (CPP) pressure 60-70 Avoid systolic BP below 110</td>
</tr>
<tr>
<td>Spontaneous intracerebral hemorrhage (sICH)</td>
<td>Systolic BP 130-140</td>
</tr>
<tr>
<td>Spontaneous Subarachnoid Hemoorhage (aSAH)</td>
<td>Systolic BP 130-140</td>
</tr>
<tr>
<td>Induced Hypertension to prevent delayed cerebral ischemia (DCI) in aSAH</td>
<td>140 Systolic</td>
</tr>
<tr>
<td>Acute Ischemic Stroke (AIS) prior to endovascular thrombectomy (EVT)</td>
<td>140-180 systolic</td>
</tr>
<tr>
<td>AIS after EVT</td>
<td>70-90 mean arterial pressure (MAP)</td>
</tr>
<tr>
<td>Deep Brain stimulation (DBS) micro and macro electrode implantation</td>
<td>120-140 systolic</td>
</tr>
</tbody>
</table>

**Neurosurgical condition** | **Source/ evidence for BP target**
--- | ---
TBI | BTF 2016 guidelines based on large retrospective data analysis
sICH | INTERACT 2 and ATTACH 2 trials
aSAH | INTERACT 2 and ATTACH 2 trials
DCI | NCT 01613235 (RCT)
AIS prior to EVT | The Society of Anesthesia and Neurocritical care (SNACC) consensus statement of 2014 and World Stroke organization 2018 guidelines
AIS after EVT | Retrospective data analysis of GOLIATH, ANSTROKE and SIESTA trials
DBS | Data from case series

**Conclusions::** The lower limit of cerebral autoregulation is considered to be 70 mm Hg
MAP and autoregulation is dynamic and narrower in acute neurosurgical conditions. Sympathetic surge is the primary reason for hypertension and therefore adherence to BP targets is essential.
SUSTAINED AXONAL DEGENERATION IN PROLONGED DISORDERS OF CONSCIOUSNESS

Sergio Bagnato, Maria D'Ippolito, Cristina Boccagni, Antonio De Tanti, Lucia Francesca Lucca, Antonio Nardone, Pamela Salucci, Teresa Fiorilla, Valeria Pingue, Serena Gennaro, Maria Ursino, Valentina Colombo, Teresa Barone, Francesca Rubino, Maria Andriolo

1Giuseppe Giglio Foundation, Unit Of Neurophysiology And Unit For Severe Acquired Brain Injuries, Rehabilitation Department, Cefalù, Italy, 2Giuseppe Giglio Foundation, Molecular Biology Laboratory, Cefalù, Italy, 3Cardinal Ferrari Center, Cardinal Ferrari Center, Fontanellato, Italy, 4S. Anna Institute, Ran (research In Advanced Neuro-rehabilitation), Crotone, Italy, 5ICS Maugeri, Institute of Pavia, Neurorehabilitation And Spinal Units, Pavia, Italy, 6Montecatone Rehabilitation Institute, ) Montecatone Rehabilitation Institute, Imola, Italy, 7ASP of Palermo, Immunohematology And Transfusion Service, Cefalù, Italy, 8Giuseppe Giglio Foundation, Rehabilitation Department, Cefalù, Italy

Background and Aims:: Sustained axonal degeneration may play a critical role in prolonged disorder of consciousness (DOCs) pathophysiology according to brain injury severity and etiology. We evaluated levels of neurofilament light chain (NFL), an axonal injury marker, in patients with unresponsive wakefulness syndrome (UWS) and in the

Methods:: This prospective multicenter blinded study involved 70 patients with prolonged DOC (12 females, mean age 39.2 ± 14.8 years) and 70 sex- and age-matched healthy controls. Serum NFL levels were evaluated by enzyme-linked immunosorbent assay at 1–3 and 6 months post-injury and compared with those of controls. NFL levels were compared by DOC severity (UWS vs. MCS) and etiology (TBI vs. HIBI). Correlations of NFL levels at study inclusion with Glasgow Outcome Scale–Extended (GOSE) scores 6 months post-injury were examined.

Results:: Patients’ serum NFL levels were significantly higher than those of controls at 1–3 and 6 months post-injury (medians, 1729 and 426 vs. 90 pg/ml; both P < 0.0001). NFL levels were higher in patients with UWS than in those in MCS at 1–3 months post-injury (medians, 2080 and 1325 pg/ml; P = 0.008) and in patients with HIBI than in those with TBI at 6 months post-injury (medians, 818 and 337 pg/ml; P = 0.037). NFL levels on study inclusion did not correlate with GOSE scores.

Conclusions:: The pronounced serum NFL elevation in patients with prolonged DOC suggests that severe brain injuries can trigger neurodegeneration with axonal damage lasting at least 6 months post-injury. This sustained axonal degeneration is affected differently over time by brain injury severity and etiology.
Background and Aims:: The aim of the scientific research is to evaluate the quality of the patient’s life (QL) in the long-term period after traumatic brain injury (TBI).
Methods:: QL was evaluated at 184 patients with long-term TBI (mild (46), moderate (61), severe (77)) according to the SF-36 scale. The average age was 42.19±0.75 years old. There were 88.9% of men. The TBI catamnesis was 6.91±0.50 years old. Anxiety and depression levels were evaluated according to HADS.
Results:: According to the SF-36 scale all life quality characteristics had significantly lower indicators (p<0.05) than control ones. The lowest rates were indicated in the components of “physical role functioning”, “emotional role functioning” and “social role functioning”. Anxiety and depression had significant correlation with all characteristics of QL. In the male group the level of depression and anxiety was inversely correlated with all SF-36 components, in the female group this was distinguished only with the indicator of “mental health” and “vitality”. It has also been stated the negative dynamics of the components “vital activity”, “general health” and “mental health” with increasing of the TBI catamnesis. The negative effect of anxiety and depression at the patients with mild TBI was predominantly on the physical component of SF-36, with moderate severity of TBI – on physical and mental component of SF-36, with severe TBI – mainly on the mental component.
Conclusions:: In the long-term period of TBI the patients rated the QL significantly below the control indicators. The dependence of individual sections on gender, catamnesis and injury severity has been determined.
ONSD/ETD AS A PROGNOSTIC RATIO OF INTRACRANIAL HYPERTENSION IN TRAUMATIC BRAIN INJURY PATIENTS IN THE EMERGENCY DEPARTMENT.

Akram Ibadi
Najdi hospital(Secours PopulaireLibanais Hospital, Emergency, nabatieh, Lebanon

Background and Aims: Our objective is to determine the ultrasonographic measurement ratio (ONSD/ETD) can accurately predict the computed tomography findings as a marker for evaluation and prognostication of intracranial pressure in traumatic brain injury.

Methods: We conducted a prospective, blinded observational study of seventy adult patients at the Department of Emergency Medicine between (2017-2018) having moderate to severe TBI and GCS <8. Using a 7.5 MHZ ultrasonographic probe on the closed eyelids, the eyeball transverse diameter(ETD) and optic nerve sheath diameter(ONSD) were performed bilaterally at the ED and after 48 hours of admission, following a 20% Mannitol infusion. ONSD/ETD ratio was calculated. Cranial CT findings (according to Marshall Classification) suggestive of elevated intracranial pressure were used to evaluate optic nerve sheath diameter accuracy.

Results: Seventy patients were enrolled. USG-ONSD was greater than 5.7 mm and decreased after mannitol infusion from 6.3(6.1–6.7) to 5.2mm(5.5–6.3)(p=0.0007). ONSD/ETD has dropped from 0.25 till 0.21(0.18–0.18). Median and Mean ETD was 22.85 mm and 22.91 ± 0.93 mm. Enlarged right/left CT-ONSDs were 6.5 ± 1.5/6.4 ± 1.3 mm at 3 mm and 6.6 ± 0.8/6.6 ± 0.6 mm at 8-10 mm from the globe (cut-off value > 5.5 mm). ONSD/ETD ratio was 0.29 ± 0.05 compared with 0.19+/-.02 in healthy adults(P<0.01). The sensitivity of ultrasonography for detection of traumatic intracranial injury found by CT was 85% (95% CI 60% to 97%) and specificity was 75% (95% CI 59% to 86%).

Conclusions: ONSD/ETD has potential as a sensitive screening test for elevated intracranial pressure in traumatic brain injury.
PROGNOSTIC SIGNIFICANCE OF HYPERNATREMIA IN ALTERED SENSORIUM

Uma Ravishankar¹, Sathyamurthy P², Philo Hazeena¹, Shankar Venkatasubramanian¹, Sundar Shanmugam¹, Radhakrishna Pedapati¹
¹Sri Ramachandra Institute of Higher Education and Research, Neurology, Chennai, India, ²Sri Ramachandra Institute of Higher Education and Research, General Medicine, Chennai, India

Background and Aims:: Early prediction of prognosis of patients in coma depends on numerous factors and remains a challenge to the physician. We sought to assess if prediction of mortality during hospital stay was improved by including clinical or biochemical parameters that could be easily obtained on arrival in the Emergency Department.

Methods:: 467 adult patients presenting to the emergency with altered sensorium were analyzed with respect to outcome at the end of hospital stay and were divided into three groups - Patients with high GCS (9-14) Patients with low GCS (3-8) Intubated patients.

Results:: Out of the total 467 patients studied, 100 died and 367 survived. The mean serum sodium in deceased patients was 136.31 mmol/L and in survivors was 132.24 mmol/L (p=0.001). The mean sodium was 131.19 mmol/L in the high GCS group, 134.95 mmol/L in the low GCS group and 137.68 mmol/L in the intubated group (p=0.000). 44.4% of patients with hypernatremia died (p=0.006). Mortality dropped to 16% with sodium <125 mmol/L. Patients with higher sodium levels had a higher mortality. In the high GCS group, mortality for high, normal and low sodium levels were 30.8%, 16.2%, 16.5% respectively. In the low GCS group, mortality for high, normal and low sodium levels were 37.5%, 24.4%, 21.8% respectively. In the intubated group, mortality for high, normal and low sodium levels were 83.3%, 37.5%, 50% respectively. In all three groups mortality was higher when serum sodium levels were high.

Conclusions:: Serum sodium levels on admission can be an independent predictor of prognosis in these patients.
Background and Aims:: Porencephaly is a cystic lesion of the brain due to an encephaloclastic insult lined by white matter, which communicates with the ventricles and/or the subarachnoid space.

Methods:: Mrs. N is a 65-year-old woman with the complaints of self-talk, hearing of unknown voices and suspecting of family members. Half a century ago, during the Liberation War of Bangladesh, one of the shells accidentally exploded in their backyard. Unfortunately, a few pieces of shrapnel penetrated her arm, leg and right side of the head. Last 50 years, she has led an almost normal life except movement difficulties and weaknesses of the upper and lower limbs. Patient sufferings have intensified gradually. She has been experiencing headaches, dizziness and vomiting. Recently, she started to forget everything. Two months back, she drank some insecticide mistakenly. She also suffered from insomnia. She talks continuously and complains about hearing unknown voices. She also started to suspect family members. She also got convulsions two or three times in the last 50 years but she didn’t take any medication for it. Her X-ray skull showed a metallic foreign body (shrapnel) lodged within her skull. Furthermore, a CT scan of the brain was advised, and there was an artifact (shrapnel) at right frontal area, extensive encephalomalacia in right cerebral hemisphere that formed porencephaly communicating with lateral ventricle. She was advised Risperidone 2mg daily and her psychosis was controlled.

Results:: Porencephaly followed by TBI is an extremely rare condition.

Conclusions:: Psychotic presentation of porencephaly is also rare. Very few case studies available in scientific Journals.
Characteristics and Assessment of Potential Concussive Events in the UEFA Champions League

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¹University College Cork, Medicine, Cork, Ireland, ²University of Toronto, Neurosurgery, Toronto, Canada

Background and Aims:: Athletes involved in elite sports such as Association Football (AF) are at a high risk of sustaining Sport-Related Concussion (SRC). The current study investigates the characteristics of potential concussions in AF, as well as the quality of subsequent assessment with respect to the International Football Association Board (IFAB) and International Conference on Concussion in Sport (ICCS) recommendations.

Methods:: Trained reviewers identified potential concussive events (PCEs) throughout 121 matches of the 2019/2020 Men’s UEFA Champions League (CL) tournament, using a standardized observation protocol. Each PCE was analyzed for visible signs of concussion and circumstantial factors, as well as assessment incidence, duration, and return-to-play decision.

Results:: In 121 matches of the 2019/2020 UEFA CL, we identified 218 PCE incidents (1.80 per match, 54.59 per 1000 match hours). Strikes to the frontal region were most likely to produce one or more signs of concussion (34.5%, n=10), followed by the temporal region (30.4%, n=14). Of the 218 PCEs, 54 (24.8%) were assessed by medical personnel, often on the sideline (83.3%, n=45). However, 73.3% (n=33) of sideline assessments were under 1 minute in length. Fifty (22.9%) players sustaining a PCE displayed one or more signs of concussion. Of these, 23 (46.0%) were assessed by medical personnel. One (2.0%) was permanently removed from play.

Conclusions:: Players suffering a PCE are occasionally assessed, often on the sideline. However, assessments rarely last longer than a minute. Players are seldom removed from play, even when visible signs of concussion are present. Improved adherence to IFAB and ICCS concussion guidelines is needed.
BACKGROUND AND AIMS:: Sports-related concussion (SRC) incidence and management within the English Premier League (EPL) is poorly described. This study's objective is to determine the contextual factors surrounding SRC and the quality of subsequent assessment with reference to the International Football Association Board (IFAB) recommendations.

METHODS:: Trained reviewers identified potential concussive events (PCEs) throughout 60 matches of the 2019/2020 Men's EPL season, using a standardized protocol. Each PCE was analyzed for visible signs of concussion and circumstantial factors, as well as assessment incidence, duration, and return-to-play decision.

RESULTS:: Through 60 matches, 67 PCE incidents were identified (1.03 per match, 33.83 per 1000 match hours). The mandibular region was found to be the most frequently affected region of the head (34.3%, n=23), with ball to head (17.9%, n=12) being the most common mechanisms of injury. Furthermore, ball to head contacts were significantly associated with one of more signs of concussion ($\chi^2=8.79$, $p<0.01$). Of the 67 PCEs, 30 (44.7%) were assessed on the sideline. However, 86.7% (n=26) of sideline assessments were under 1 minute duration. Thirty (44.8%) players sustaining a PCE displayed one or more signs of concussion. Of these, 20 (29.9%) were assessed by medical personnel. Only one (3.3%) player was permanently removed from play.

CONCLUSIONS:: Unfortunately, players suffering PCE are occasionally assessed on the sideline. However, assessments are typically less than a minute in duration and rarely result in permanent removal from play despite the presence of visible signs of concussion. As such, PCE identification and management during matches remains insufficient with respect to international recommendations.
PROGNOSTIC FACTORS RELATED TO THE RISK OF COVID-19 INFECTION IN MS PATIENTS

Federico Montini¹, Agostino Nozzolillo¹, Lucia Moiola¹, Maria Rocca¹,²,³,⁴, Vittorio Martinelli¹, Massimo Filippi¹
¹IRCCS San Raffaele Scientific Institute, Neurology Unit, Milano, Italy, ²IRCCS San Raffaele Scientific Institute, Neuroimaging Research Unit, Division Of Neuroscience, Milan, Italy, ³Vita-Salute San Raffaele University, Na, Milan, Italy, ⁴Ospedale san Raffaele, Neurology, Milano, Italy

Background and Aims:: It is still debated whether Multiple Sclerosis (MS) patients are at high-risk of COVID-19 because of their life style, disease- or treatments-associated immune alterations. We compared features of MS patients with COVID-19 infection (MS-COVID) to those of residency-, age-, sex- and treatment-matched MS controls (MS-NCOVID). Moreover, the severity of COVID-19 infection was assessed in MS-COVID patients and their cohabitants.

Methods:: So far, we have enrolled 25 MS-COVID and 104 MS-NCOVID patients. Neurological examination, premorbid laboratory tests, anthropometric variables (height, weight and BMI), life-style habits (smoke, alcohol intake, diet), working-activity and living conditions (number of cohabitants, school-aged children) were assessed. COVID-19 severity was evaluated in terms of fever (magnitude, duration), radiological pneumonia and typical symptoms.

Results:: Clinical and anthropometric features, life-style habits and living conditions were similar between MS-COVID and MS-NCOVID patients. However, they differed in terms of working activity, with lower rate of unemployment (7.1% vs 23.4%) and higher rate of team-working (61.5% vs 26.5%) in the MS-COVID group (p<0.01). Furthermore, MS-COVID patients had lower premorbid vitamin D levels (31 vs 40 ng/ml p=0.048) and higher neutrophils count (3803 vs 3182 cells/ul, p=0.046). Disease course was similar between MS-COVID patients and their cohabitants with fever, ageusia and anosmia being the most common symptoms. Fever and radiologic signs of pneumonia were also comparable.

Conclusions:: Working-activity, lower vitamin D levels and higher neutrophil count seem to be associated with the risk of COVID-19 infection in MS patients. The burden of COVID-19 disease was comparable between MS patients and their cohabitants.
Background and Aims:: The frequency of Huntington's disease (HD) may vary considerably, with higher estimates in non Asian populations. Here we present two studies performed in Sardinia, a large mediterranean island that's considered a genetic isolated: a study of HD incidence over a ten-years period, 2009 to 2018, in overall Island, and a prevalence study in the southern part of it.

Methods::

Methods. Our research was conducted in the 5 administrative areas of Sardinia island (fig1). Case-patients were ascertained through multiple sources in Sardinia and Italy.

Results:: Results. During the incidence period 53 individuals were diagnosed with clinically manifested HD. The average annual incidence rate 2009 - 2018 was 2.92 x 10^6 persons - year (95% CI, 2.2 to 3.9). The highest incidence rate was observed in South Sardinia (6.3; 95% CI, 4.2 – 9.5). This rate was significantly higher (p<0.01) than the rates from Cagliari, Oristano, and Sassari provinces but did not significantly differ (p = 0.38) from the Nuoro rate. The resulting prevalence rate was 5.98 x 10^5 in the
overall study area, however with marked variations between South Sardinia and Cagliari (9.6 x 10^5 vs. 3.0 x 10^5, p=0.02). In the study areas, we found similar CAG repeat length in normal alleles.

**Conclusions:** The overall epidemiology of HD in Sardinia is close to the correspondent estimates in Mediterranean countries. Our findings highlight also the possibility of local microgeographic variations in the epidemiology of HD that might reflect several factors, including a possible founder effect in the rural areas of South Sardinia and Nuoro.
BURDEN OF NEUROLOGICAL DISORDERS IN EUROPE: AN ANALYSIS BASED ON THE GLOBAL BURDEN OF DISEASE 2017

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\textbf{Background and Aims::} Neurological disorders, together with other Non-Communicable Diseases (NCDs) such as mental health, musculoskeletal, cardiovascular disorders and tumors, account for 65.5\% of the burden associated to NCDs at the global level.

\textbf{Methods::} We relied on estimates referred to Prevalence, Deaths, Years of Life Lost (YLLs), Years Lived with a Disability (YLDs) and Disability-Adjusted Life Years (DALYs) taken from the 2017 wave of the Global Burden of Disease (GBD) study, and referred to 31 European countries.

\textbf{Results::} Neurological disorders prevalence was 256.0 million, i.e. 59.2\% of all NCDs, and they caused 1.1 million deaths (23.5\% of all NCDs). Neurological disorders accounted for 12.5 million YLLs (18.2\% of all NCDs), 9.6 million YLDs (16\% of all NCDs) and 22.2 million DALYs (17.2\% of all NCDs). Headache disorders and stroke were the most prevalent and disabling conditions, whereas stroke and dementias were those associated to higher mortality and YLLs. In terms of DALYs, stroke, dementias and headache disorders were the most burdensome conditions, as they accounted respectively for 5.7\%, 4.2\% and 3.7\% of DALYs attributable to NCDs in Europe.

\textbf{Conclusions::} Neurological disorders are the most prevent conditions in Europe and rank second for DALYs after tumors. The burden of neurological diseases has increased in absolute terms since 2010, mostly in reason of the dramatic explosion of the DALYs associated to headaches, stroke, Parkinson’s disease and dementias (increase rates between +145\% and +500\%). In consideration of ageing trends, public health strategies are needed to identify the best caring practices.
POST HERPETIC NEURALGIA - A STUDY OF DEMOGRAPHICS IN COSMOPOLITAN TERTIARY CENTRE IN PENANG, MALAYSIA

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Background and Aims:: Post Herpetic Neuralgia (PHN) is a complication of VZV reactivation which remained latent in ganglion of cranial nerves, dorsal root and autonomic nerves. It is characterized by persistent pain, leading to significant psychosocial impact. The study intends to investigate the demographics of patients and sites of PHN in Penang Hospital.

Methods:: The study involves a retrospective analysis of patient diagnosed with PHN from the year 2007 to 2020.

Results:: 88 patients were identified to have PHN, consisting of 42 (48%) male and 46 (52%) females, with a female preponderance. Most cases (49%) occurred among individuals from 61 to 70 years old. The left sided PHN is slightly more common than the right accounting for 45 (51%) and 43 (49%) cases respectively. The pain commonly involves the thoracic dermatomes 43 (48%) cases followed by trigeminal nerve distribution involving 26 (29%) individuals, 19 (22%) patients have underlying hypertension, 13 (15%) have diabetes mellitus and 10 (11%) have underlying malignancy.
Conclusions: Our study has suggested that PHN commonly affects individuals from the age 61 to 70 years old and the thoracic dermatomes. In our study, approximately 26% of patients were diagnosed with immunocompromising diseases such as diabetes and malignancy, which prompted speculation on neuroimmunology etiology of PHN. In conclusion, the treatment strategy and cure for PHN remained limited. Most patients with PHN and trigeminal neuralgia remain medication dependent. Thus, the effort in addressing the burden of PHN should be focused on acute herpes zoster preventions as well as the holistic approach involving multidisciplinary teams with east west integration.
INCIDENCE AND DISTRIBUTION OF PRIMITIVE CNS TUMORS IN SOUTHERN SARDINIA, 2016-2019

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Background and Aims:: CNS tumors (CNST) carry a substantial source of morbidity and mortality in the world, but epidemiological data are poor. This study evaluated the incidence of primitive CNST in the adult population of Southern Sardinia over a four-year span and identified incidence clusters over the area under study.

Methods:: Adult patients with CNST were identified by examining the computerized database of the Departments of Neurology, Neurosurgery, Pathology and Oncology of the five hospitals localized in the study area (Cagliari Metropolitan Area and South Sardinia (SU) province). We excluded secondary tumors of the CNS, meningiomas and tumors of cranial and paraspinal nerves. Cluster analysis was performed by age- and sex- adjusted Kulldorf's spatial scan statistic (KSSS).

Results:: Histological diagnosis was available in 199/234 patients (85%). Crude incidence of CNST was 7.4/100000 persons-year and the age-adjusted standardized rate (AASR) was 6.2/100000 persons-year. Glioblastomas showed a crude incidence rate of 5.7/100000 persons-year and an AASR of 4.7/100000 persons-year. The Cagliari and SU provinces showed comparable CNST (7.1 versus 7.8/100000 person-years; p = 0.5) and glioblastomas rates (6.0 versus 4.9/100000 person-years; p=0.2). The KSSS did not reveal any incidence cluster related to the CNST overall. Considering only glioblastomas, were detected a low-incidence cluster and a non-significant high-incidence cluster.

Conclusions:: Our CNST incidence rates were similar with previous studies while our glioblastomas incidence rates tended to be higher than other European data. The population of the aforementioned clusters needs to be evaluated in further investigations, inquiring for risk or protective factors.
THE EVALUATION OF THE PAIN, STRESS AND PHYSICAL ACTIVITY ACCORDING TO THE ERGONOMIC CONDITIONS IN THE WORKPLACE OF THE ACADEMIC STAFF

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Background and Aims:: This study was conducted to examine the pain, stress and physical activity according to the ergonomic conditions in their workplace of academic staff.

Methods:: Eighty-five academic staff working at Suleyman Demirel University participated in the study. The International Physical Activity Questionnaire – Short Form (IPAQ- SF) was used to determine the physical activity levels of the participants, Nordic Musculoskeletal Questionnaire (NMQ) to determine their pain, and the Perceived Stress Scale (PSS) to determine their stress levels. A Rapid Office Strain Assessment (ROSA) was conducted to determine the ergonomic condition of the workplace.

Results:: According to the analysis, statistically significant differences were found between academic personnel with and without the ergonomic environments in their workplace in terms of total scores of the IPAQ-SF (p = 0.018). In addition, it was observed that there is not a significant difference between these groups in terms of PSS score (p > 0.05). The percentage of neck pain was higher than back pain in academic personnel.

Conclusions:: According to the result, the ergonomic conditions of the workplace affected individuals’ physical activity level but not stress level. In addition, academic staff in University could be considered as a risk group of job-related neck pain.
WHAT IS AMYOTROPHIC LATERAL SCLEROSIS PREVALENCE?

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Background and Aims:: ALS prevalence ratio is usually calculated excluding prevalent cases. This may lead to a methodological bias, given the high variability of ALS patients survival, mostly according to phenotype. We aimed at assessing ALS prevalence and to evaluate how the historical depth of data may influence the prevalence ratio estimate.

Methods:: Data from the PARALS Register were used. Crude prevalence ratio was estimated on December 31, 2015 for the period 2015-2013 and then repeated extending the time interval by three years each time. For each time interval, prevalence ratio was calculated globally and stratified by sex, age at diagnosis, and phenotype. Prevalence was also calculated considering patients who underwent tracheotomy during the same period.

Results:: Prevalence ratios increased proportionally to the length of the time period considered, ranging from 6 (95% CI 5.3 - 6.7) for a 3-year period to 12.1 (95% CI 11.1 - 13.1) per 100.000 for 21-year period. Respiratory phenotype did not contribute to the increase of prevalence ratio as time periods lengthened (from 0, 95% CI 0 - 0.2, to 0.1, 95%CI 0 - 0.3). Conversely, predominant UMN showed the highest increase (from 0.5, 95% CI 0.3 – 0.8, to 2.1, 95% CI 1.7 – 2.6, +320%).

Conclusions:: the depth of data collection influences the prevalence ratio estimate. A 12-year period should be sufficient to get a reliable evaluation of ALS prevalence including long-survival patients. This results may be useful in assessing predictive values of prognostic markers but also in planning health resources, given the significant social and assistential burden of the disease.
RECOMPRESSION OF SPINAL CORD DECOMPRESSION SICKNESS

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Background and Aims:: Symptoms of spinal cord decompression sickness(DCS) occur almost immediately when out of water. It is recommended that recompression treatment should be performed soon in order to avoid further tissue injury. Unfortunately, there may be a significant time delay from surfacing to recompression. The aims of the study were to evaluate the effect of delayed hyperbaric treatment, initiated more than 30hr after surfacing for DCS and to evaluate the different treatment protocols.

Methods:: 68 injured divers presenting symptoms of spinal cord DCS were retrospectively included from Seoul Medical Center. Diving information, time interval between symptom onset and hyperbaric treatment were studied. The initial severity of spinal cord DCS was rated with the Boussuges severity score and muscle power examination and the presence of sequelae was evaluated at 2 weeks. Initial recompression treatment at 2.8 - 4 ATA (atmospheres absolute) with 100% oxygen breathing or deeper recompression.

Results:: There were no significant differences between each group in age, diving experience, depth of dive. bottom time of dive, Boussuges's score. With respect to treatment results, at the delayed treatment divers, good recovery was achieved in 47.1% of the divers. When treatment started early, good recovery was achieved in 58.8% of the divers. Hyperbaric treatment using US Navy Table6a protocol trended toward a better clinical outcome, statistically significant (p=0.04) compared to US Navy Table6.

Conclusions:: The prognosis is good when the recompression therapy is delayed in patients with spinal decompression sickness. Hyperbaric oxygen treatment is better in US Navy Table6a than Table6 in patients with spinal decompression sickness.
TOBACCO USE AND HEALTH: PERCEPTION AND PRACTICE AMONG TEENAGER STUDENTS OF TELANGANA STATE INDIA.

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Background and Aims:: Background & aims: Tobacco related diseases (cancer, heart & brain stroke) cause 20 millions death per year. Out of these 2/3rd death occur in China and India. There is urgent need to identify the target population and implement effective policies for prevention of tobacco use. Aim of study was to identify the prevalence and level of knowledge among high school students of tobacco use and the factors influencing their act for early intervention.

Methods:: A cross-sectional survey was done on 1000 high school students in the age group of 14 to 16 years from rural area of Warangal, and Jangaon, districts of Telangana state, India from June 2019 to December 2019. This survey was done by epidemiologist of TNC medical foundation (A Registered Non-Governmental organization).

Results:: 600 boys and 400 girls were interviewed through a prepared questionnaire. Among study group, 20% accepted smoking habit (95% boys and 5% girls). Various reasons were cited for smoking and tobacco chewing e.g. fun and enjoyment (20%), imitation of the action hero of the popular movies (25%), to alleviate the boredom etc. 80% knew the content and toxic effect of tobacco on health. 64% students wish to stop smoking. 75% students want ban on tobacco products (cigarettes, ghutka ) use in public places by the government.

Conclusions:: Conclusion: Majority of the students had the knowledge of tobacco toxicity. Student counseling, health education and awareness programs by trained professionals at school stage should be planned by the government to reduce tobacco related death in developing countries.
THE PREVALENCE OF LOWER URINARY TRACT SYMPTOMS IN PATIENTS WITH MULTIPLE SCLEROSIS IN RIYADH, SAUDI ARABIA

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Background and Aims:: Exploring the prevalence of lower urinary tract symptoms (LUTS) in multiple sclerosis (MS) patients may lead to optimizing therapeutic interventions that could improve their quality of life (QoL). The main objective of this study was to assess the prevalence of LUTS in patients with MS in Riyadh, Saudi Arabia.

Methods:: This cross-sectional study targeted Saudi nationals aged 18-50 who were previously diagnosed with MS and presented with urinary tract dysfunction symptoms. It was conducted from November 2020 to January 2021 through the distribution of a self-administered electronic questionnaire.

Results:: Data were collected from 158 patients with MS. Most participants (44.3%) were between 30 and 39 years old, and 64.6% were female. The severity of LUTS is significantly associated with the QoL of patients, where an increase in severity of LUTS would worsen their QoL (p < 0.001). More than half of the sample (52.5%) indicated that they had taken treatment for these symptoms, 40.7% of whom reported using medicinal treatment. The duration of illness, age, or gender was found to have no significant effect on LUTS severity.

Conclusions:: We found that LUTS and urinary incontinence prevalence among patients with MS do not significantly correlate with different genders and age groups. LUTS seem to have a significant negative impact on the QoL of patients with MS.
Background and Aims:: Neglected tropical diseases (NTDs) are a set of 20 diseases classified by WHO that affect populations with low access to health services. In 2012, Brazil took part in the “London Declaration on NTDs”, an international partnership to combat 10 NTDs by 2020. All NTDs in Brazil may have neurological manifestations, so it is essential to know about the epidemiology and clinical implications.

Methods:: An observational, retrospective and epidemiological study based on available data of the Department of the Unified Health System obtained through the application Health Information. We evaluated the absolute means of incidence in two groups (2007-2013 and 2014-2020), it was organized and analyzed based on statistical methods. The neurological manifestations of NTDs were searched in literature.

Results:: These NTDs appeared in the London Declaration: leprosy, trachoma, schistosomiasis, soil-transmitted helminthiasis, Chagas disease, visceral leishmaniasis, and onchocerciasis. Trachoma and onchocerciasis are not mandatory notification diseases, and epidemiological data is scarce in Brazil. Leprosy, schistosomiasis (data until 2017) and helminthiasis had decreased incidences. Chagas disease (data up to 2019) incidence increased by 95.25% in national data - and there is no report in Paraná. Visceral leishmaniasis increased (data up to 2019) in Paraná by 138.81%, and its incidence decreased by 1.82%. The neurological manifestations may be stroke, neurological injury, meningoencephalitis, myelopathy, neuropathy, and death due to neurological damage.

Conclusions:: Although incidences of NTDs have fallen, Brazil has not met the deal agreed in 2012, furthermore, it has reduced investments to combat these diseases. The neurological manifestations of NTDs have significant implications for morbidity and mortality.
Background and Aims:: Patients with Parkinson’s disease have higher rates of hospital admissions and longer length of stay than patients without the disease. This study aims to evaluate the epidemiology of hospitalizations for Parkinson’s disease in Brazil during 2019 and 2020.

Methods:: Cross-sectional, descriptive and retrospective study, which evaluated the epidemiology of hospital admissions for Parkinson’s disease in the Brazilian National Health System in the years 2019 and 2020. Hospital admissions were evaluated by sex, race, and age group using the national database (DATASUS – Department of Informatics of the Unified Health System).

Results:: During this time period, there was a total of 1623 hospitalizations for Parkinson’s disease in the Brazilian National Health System, with 947 (58.4%) hospital admissions in 2019 and 676 (41.6%) in 2020. Also, 972 (59.9%) patients were male and 651 (40.1%) were female. Regarding race (n=1299); 777 (59.8%) patients considered themselves white, 442 (34%) brown, 54 (4.2%) black and 26 (2%) others. Regarding age groups; 278 (17.1%) were >80 years old, 847 (52.2%) were 60-79, 453 (27.9%) were 40-59 and 45 (2.8%) were <40.

Conclusions:: The majority of patients hospitalized for Parkinson’s disease were male, white, and 60-79 years old. There was a decrease in hospital admissions for Parkinson’s disease from 2019 to 2020, which may be related to the hospital’s oversaturation by COVID-19. In addition to that, the disease is still little analyzed epidemiologically in the country and needs more attention.
HOSPITAL ADMISSIONS FOR BACTERIAL MENINGITIS DURING 2019-2020 IN BRAZIL

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Background and Aims:: Bacterial meningitis is a prevalent concern in low and middle-income countries, accounting for a high number of deaths and hospitalizations. This study aims to evaluate the epidemiology of hospitalizations for bacterial meningitis in Brazil during 2019 and 2020.

Methods:: Cross-sectional, descriptive and retrospective study, which evaluated the epidemiology of hospital admissions for bacterial meningitis in the Brazilian National Health System in the years 2019 and 2020. Hospital admissions were evaluated by sex, race and age group using the national database (DATASUS – Department of Informatics of the Unified Health System).

Results:: There was a total of 6921 hospitalizations for bacterial meningitis, being 4091 (59.1%) from 2019 and 2830 (40.9%) from 2020. In addition, 3922 (56.6%) patients were male and 2999 (43.4%) were female. Regarding race, 2421 (35%) considered themselves white, 2710 (39%) brown, 275 (4%) black, 130 (2%) yellow, 31 (0.5%) indigenous and 1354 (19.5%) did not have skin color informed. Regarding age groups; 1156 (16.7%) were <1 year old, 796 (11.5%) were 1-4, 560 (8.1%) were 5-9, 439 (6.3%) were 10-19, 818 (11.8%) were 20-29, 730 (10.5%) were 30-39, 641 (9.3%) were 40-49, 625 (9%) were 50-59, 436 (6.3%) were 60-69, 209 (3%) were 70-79, 85 (1.3%) were >80.

Conclusions:: The majority of patients hospitalized for bacterial meningitis disease were male, brown and <1 year old. There was a decrease in hospital admissions for bacterial meningitis from 2019 to 2020, which may be related to the increased social isolation due to COVID-19.
A NOVEL WDR45 MUTATION IN A 6-YEAR-OLD BOY WITH AUTISM, LENNOX-GASTAUT SYNDROME, AND ADHD

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Background and Aims:: Beta-propeller protein-associated neurodegeneration, i.e., neurodegeneration with brain iron accumulation type 5, is due to mutations in the WDR45 gene. We report a case where a novel pathogenic mutation was discovered.

Methods:: Case Report

Results:: A 6-year-old boy presented with autism, developmental delay, seizures, and aggression. Details of his birth history were unknown. He had been on levetiracetam since 3. His parents first witnessed near-daily drop attacks. Valproic acid was added to toleviracetam, which resolved his drop attacks but head banging increased, hence discontinued. He was 117cm (7th percentile) and weighed 23.5kg (39th percentile). Head circumference was 50cm (17th percentile). He was not dysmorphic, but very hyperactive and disruptive. EEG was indicative of Lennox-Gastaut syndrome. MRI showed neurodegeneration with iron accumulation. Amphetamine-dextroamphetamine and Methylphenidate for ADHD did not help. Levetiracetam was increased and valproic acid was restarted, which had resolved his seizures. Risperdone was started for aggression. Genetic testing revealed a novel pathogenic variant (c.577C>T, p.Gln193) in WDR45. Allele fraction was 46%, suggesting mosaicism. At 8 his verbal communication improved, and he was seizure-free.

Conclusions:: A novel pathogenic variant (c.577C>T, p.Gln193) was found in the WDR45 gene as a mosaic with an allele fraction of 46%. The clinical features of our case were unique; he clearly did not have cerebral palsy nor was he bedridden. To date, at age 8, he still does not exhibit any signs of parkinsonism or dystonia. Whether this was due his mosaicism or the specific novel mutation remains unclear. Postzygotic mosaicism might explain why his phenotype was not as severe.
Background and Aims:: Single nucleotide polymorphism (SNP) HTR1A C1019G (rs6295) is located in promoter area and binds the NUDR / Deaf1 transcription factors with different affinities, which result in the level change of gene transcription. Minor allele G is associated with mental disorders, the development of depression, post-traumatic mental disorders, and resistance to anti-psychotic drugs. The aim of our study was to investigate the contribution of the SNP to development of neurological disorders in patients with neuro ICU.

Methods:: Study cohort included 134 neuro ICU patients with trauma, anoxic brain injury and brain tumors. HTR1A rs6295 polymorphism was studied by using an HTR1A specific oligonucleotide tetraprimer set. The content of oxidized DNA was determined using immunoassay.

Results::
Nihss (scale of neurological disorders) values on days 1 and 5 were significantly lower in patients with CC genotype compared to G carriers (16 vs. 18, $P=0.025$ and 15 vs. 18, $P=0.024$, respectively, $N=134$). Unexpectedly, we found association HTR1A rs6295 genotypes with concentration of oxidized DNA fragments (but not all cell-free DNA) in the plasma of patients. In patients carrying the G risk allele, the amount of oxidized DNA in plasma was lower (191 vs. 645, $P=0.03$ $N=63$). Thus, the low oxidized DNA value in plasma appears a significant unfavorable marker for neuro ICU patients.

**Conclusions:** G allele HTR1A rs6295 is associated with increase of neurological disorders in the group of neuro ICU patients with tumors, trauma, and anoxic brain injuries.
CLINICAL AND GENETIC FEATURES OF A LARGE COHORT OF ITALIAN SPG4 PATIENTS FROM THE D.A.I.S.Y. COLLABORATIVE NETWORK.

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Background and Aims:: Hereditary spastic paraplegias (HSPs) are rare, inherited neurological disorders, characterised by degeneration of the corticospinal tracts and dorsal columns. SPG4, caused by heterozygous mutations of the SPAST gene, represents the most common form. Herein, we present findings from the largest described cohort of Italian SPG4 patients, aiming to define the clinical spectrum of SPG4 in Italy, and find any significant genotype-phenotype correlations.

Methods:: We retrospectively collected clinical and molecular data from 723 patients (419 males, 58%) from 316 families. Family history for SPG4, age at onset (AAO), disease severity by SPATAX disability and SPRS scales were gathered from medical records. Numerical and categorical variables were analyzed by Mann-Whitney and Chi-squared test, respectively.

Results:: Overall, penetrance of SPG4 was 0.98. Mean AOO was 32.46±17.41 years, with a bimodal distribution (Fig.
Males showed more frequently spastic gait (96.9% vs 90.2%) with a higher SPRS score (19.56 vs 16.18), and were more frequently assuming myorelaxant drugs (70.1% vs 59.3%). Overall, 186 different SPAST mutations were recorded (Fig. 2).
Compared to truncating mutations, patients with missense mutations had more frequently intellectual deficiency. On the other hand, patients with truncating mutations showed more frequently spasticity at rest, lower limbs proximal weakness, urinary disturbances, polyneuropathy, cerebral atrophy, and cognitive decline (Fig. 3).

**Figure 2.** Frequency of the different *SPAST* mutations found in our cohort (n=186).
Conclusions:: We documented a more severe motor involvement in males, and a more diffuse disorder in patients carrying truncating mutations. This wide multicenter study allowed to define phenotypic and genotypic spectrum of SPG4 in Italy, creating a network addressing SPG4 patients to hopefully forthcoming clinical trials.

**Figure 2.** Comparison of clinical and diagnostic findings between truncating and missense mutations' carriers (only significant ones shown, p<0.05).
MULTIPLE SCLEROSIS ASSOCIATED HLA VARIANTS AFFECT THE IMMUNOLOGICAL T LYMPHOCYTES REPERTOIRE

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Background and Aims:: Multiple sclerosis (MS) is a neurodegenerative and autoimmune disorder in which genetic predisposition plays an important role, with the major histocompatibility complex (MHC) region accounting for 32 independent associations. We aim to investigate the impact of MHC MS-risk alleles on T-lymphocytes repertoire in MS patients.

Methods:: 183 untreated relapsing-remitting MS subjects have been studied. Class I and II HLA alleles were inferred from whole-genome genotyping data using SNP2HLA and Beagle_v3.3 tools. T-cell receptor (TCR) CDR3 sequences were obtained from whole blood DNA according to the ImmunoSEQ hsTCRB kit (Adaptive Biotechnologies®). A weighted HLA-risk score (wHRS) was calculated. The inverse of the Simpson’s Index (INV.S) was calculated as representative of immune repertoire diversity. Statistical analyses were performed within R environment and plink v.1.9.

Results:: The final set was composed by 144 individuals and 30 MS-risk MHC loci. Four loci showed association with INV.S: HLA DRB1*15:01 (P=0.014), rs11751659 (P=0.02), rs9271366 (P=0.003), SNP_DRB1_32660116_A (P=0.036). A mild association was found between INV.S and wHRS (P=0.049), with individuals with a higher wHRS showing a lower diversity. Moreover, individuals carrying the risk alleles showed a different percentage of clonotypes occupying the 10% of the repertoire with a set of clonotypes enriched only in MS-risk HLA carriers that were identified.

Conclusions:: MS-risk MHC loci appear to influence TCR repertoire in MS patients, with the risk alleles reducing the diversity and inducing an expansion of specific clonotypes. Analyses are ongoing to better define the amplified clonotypes and their role.
EXTRA-REPEAT INSERTIONAL MUTATION IN THE PRNP GENE WITH CEREBRAL AMYLOID ANGIOPATHY: A CASE REPORT

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Background and Aims:: Cerebral amyloid angiopathy (CAA), a major cause of spontaneous intracerebral haemorrhage and cognitive decline, has been documented in some forms of prion diseases (PrDs). Octapeptide Repeat Insertions (OPRIs) in the prion protein gene (PRNP) are mutations associated with genetic prion diseases (gPrDs). This is the first report of a patient with rapidly progressive dementia, carrying one OPRI in the PRNP gene and neuroimaging features consistent with CAA.

Methods:: We evaluated an 80-year-old man with no family history of neurodegenerative disease for cognitive impairment. Brain MRI, EEG-EMG polygraphy and analysis of Amyloid Precursor Protein gene (APP), Presenilins (PSEN1 and PSEN2) and PRNP gene were performed. 14–3–3, Tau proteins and Aβ42 were assessed in the cerebrospinal fluid (CSF).

Results:: The patient had cognitive dysfunction, abulia, postural limb myoclonus and unsteady wide-based gait. About 9 months after onset, he was bed-bound, almost mute and akinetic. Brain MRI showed sequelae of intraparenchymal haemorrhage, microbleeds and cortical siderosis, consistent with CAA. Genetic tests revealed the presence of one OPRI (24 bp insertion) in the coding region of PRNP. CSF had high Tau and p-Tau, decreased Aβ42 and absent 14.3.3 protein. EEG-EMG polygraphy showed diffuse slowing, bilateral frontal theta activity and generalized spikes-waves related to upper limb myoclonus induced by intermittent photic stimulation.

Conclusions:: To our knowledge, this is the first report of a patient with rapidly progressive dementia with detection of one OPRI in the PRNP gene and CAA. Although one OPRI is of questionable pathogenicity, our observations raise the question whether these two findings are causally linked.
AN ATYPICAL CASE OF SPASTIC PARAPLEGIA TYPE 11 MIMICKING A GM2 GANGLIOSIDOSES

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Background and Aims:: Spastic paraplegia type 11 (SPG11) is the most frequent autosomal recessive HSP. SPG11 patients' fibroblasts and mouse models revealed endolysosomal system dysfunction; endolysosomal lipid accumulation, especially gangliosides, was observed in post-mortem brains. We report an atypical patient with clinical onset and biopsy findings mimicking a GM2 gangliosidoses.

Methods:: A clinical, biochemical and metabolic characterisation was performed from the childhood, in the late 1980's, to the adulthood. Electron microscopy analysis was performed on rectal mucosa and skin biopsy specimens. A NGS panel including 154 genes associated to neuronal ceroid lipofuscinosis and HSP was performed.

Results:: The patient presented with worsening walking difficulty and psychomotor slowdown since childhood. In the late childhood, to exclude a neurometabolic storage disease, skin and rectal biopsy was performed: enteric neurons showed lipofuscin-like intracellular inclusions thus suggesting a possible GM2 gangliosidoses. However, the GM2A gene sequencing and the lysosomal enzymatic assay did not allow to confirm such hypothesis. In adulthood we detected flaccid paraplegia, distal hypotrophy, reduced deep tendon reflexes and horizontal gaze nystagmus. Further analysis revealed axonal motor neuropathy, carpus callosum atrophy and colon atony. Surprisingly, the NGS panel detected two already reported SPG11 mutations in a compound heterozygous state.

Conclusions:: We describe the atypical clinical and pathological features of a genetically ascertained SPG11 patient. For the first time we detected pathological hallmarks in enteric neuron from a rectal mucosa biopsy. The report thus illustrates the possible overlap between SPG11 and GM2-Gangliosidosis, especially in the first disease phases, and helps to improve our knowledge about SPG11 physiopathology neurodegeneration.
DCTN1 VARIANTS’ ROLE IN NEURODEGENERATIVE DISEASES: A REGIONAL TWO-CENTERS EXPERIENCE.

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Background and Aims:: The DCTN1 (dynactin 1) gene encodes for the major subunit of the dynactin protein complex which plays a crucial role in axon maintenance and organelles and vesicle transport regulation. Variants in this gene have been associated with various neurodegenerative disorders, most notably Perry syndrome, but also other types of parkinsonism, FTD, ALS and inherited neuropathies. In this work, we screened for DCTN1 variants a population of 607 patients referred to two centers of the Emilia Romagna region (Italy) affected by various type of neurodegenerative disorders, to define prevalence and clinical features associated with these variants.

Methods:: 607 patients affected by different neurodegenerative disorders for which a genetic origin was suspected (because of familiarity, early age of onset or peculiar phenotype) underwent genetic testing via a custom Next Generation Sequencing panel including the DCTN1 gene.

Results:: We identified 13 rare variants of the DCTN1 gene that were predicted to be pathogenic or likely pathogenic by at least one of the three different in-silico tools used for deleteriousness prediction (9 of them by 2/3 of the tools). The predominant clinical presentation was cognitive impairment (77%), particularly bvFTD, often associated with parkinsonism (31%). Two patients (15%) presented only with atypical parkinsonism, and one (8%) with isolated progressive lower motor neuron disease.

Conclusions:: Variants in DCTN1 gene are a rare but unneglectable cause of neurodegenerative disorders, with protean manifestations, and this gene should be included in the extensive search for genetic variants in different phenotypes.
Background and Aims:: The Global Parkinson’s Genetics Program (GP2) is an international collaborative effort aiming at improving knowledge on genetics in Parkinson’s disease (PD). The “Monogenic Hub” plans to perform whole-genome sequencing (WGS) for a total of 5-10,000 PD patients over a period of 5 years, to discover novel monogenic PD causes and better characterize genetic modifiers influencing disease manifestation and progression. We aim to develop an easy-to-use online platform for case/family submission to support the efforts of GP2.

Methods:: Researchers with expertise in PD genetics collaborated with web designers and developed a registration site to submit information regarding institutional ethical clearance for international data and sample sharing, as well as an electronic case report form to submit pseudonymized data of patients/families in whom a monogenic cause of PD is suspected. To maximize participation, especially from underrepresented populations, clinical and available genetic pre-screening datasets are designated as “Minimal”, “Core” and “Extended”. All submitted cases will undergo comprehensive genotyping with the Illumina Global Diversity Array.

Results:: The Monogenic Hub website, including the Monogenic Portal (https://monogenic.gp2.org), was launched on February 8th, 2021. Feedback received from users is continually used to further refine the accessibility/user-experience of the platform. A video tutorial was also created to help the submitters during their first registration to the Monogenic Portal.

Conclusions:: We established an online platform for case/family submission within the “Monogenic Hub” of GP2. The collection of rich patient/family data will facilitate prioritization of samples for WGS, enable deeper analysis of genetic, clinical-demographic and environmental factors influencing disease expression.
THE GLOBAL PARKINSON’S GENETICS PROGRAM (GP2): THE MONOGENIC HUB 500-GENOMES PILOT PROJECT

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Background and Aims:: The Global Parkinson’s Genetics Program (GP2) is an international collaborative program that focuses on improving our understanding of the role of genetics in Parkinson’s disease (PD) and on making this knowledge globally available and actionable. The “Monogenic Hub” aims to perform both short and long-read whole-genome sequencing (WGS) for a total of 10,000 PD patients starting with a 500-genomes pilot project, with the goal of identifying novel monogenic causes of PD.

Methods:: Clinical and pre-existing genetic data on patients from around the globe were obtained through online questionnaires and are further collected through the Monogenic Portal, an easy-to-use online application. All submitted cases were evaluated and prioritized for pilot WGS based on the following criteria: number of affected family members and sample availability, pedigree structure, consanguinity history, early age at onset (AAO) and availability of genetic prescreening. A particular focus was placed on currently underrepresented populations in genetic studies.

Results:: 16 research teams from 10 different countries submitted 757 PD patients to the Monogenic Hub. We selected 512 cases for our 500-genomes pilot; 75% of them were familial cases and the remaining were singletons with an AAO ≤ 40 years. The majority had negative genetic pre-screening and ~20% are from underrepresented populations.

Conclusions:: Within the Monogenic Hub of GP2, we established a screening process and an online platform for case/family submission allowing us to perform WGS for the first 500 PD patients from 279 families with an as yet unknown but suspected monogenic cause of their PD.
Background and Aims:: Leukodystrophies are genetic neurological disorders characterized by involvement of the white matter of the CNS that may occur at all age. The ovarioleukodystrophies comprise a group of rare leukodystrophies associated with primary or premature ovarian failure.

Methods:: A case report to determine the clinical and radiological characteristics of ovarioleukodystrophy.

Results:: A 44-year-old woman presented with progressive difficulties in walking during the last 3 years. Her medical background showed spaniomenorrhea and infertility and she had no familial medical history. Neurological examination showed depression, dementia and bilateral pyramidal weakness. On biology, she had ovarian failure with low estrogen levels and high LH and FSH levels with undetectable ovaries on pelvic ultrasonography. Brain magnetic resonance imaging (MRI) revealed diffuse and symmetric white matter abnormalities with lesions having cerebrospinal fluid-like signals. The diagnosis of ovarioleukodystrophy was made on the basis of Van Der Knaap criteria.

Conclusions:: Ovarioleukodystrophy is an association of adult-onset vanishing white matter disease and premature ovarian insufficiency (POI). It is a rare autosomal recessive leukoencephalopathy caused by mutations in any of five genes encoding the eukaryotic initiation factor 2B (EIF2B1–5). The mean age of clinical onset in female patients is 36.8 years. The symptoms may combine progressive subcortical cognitive decline with behavioural disorders and motor signs. Ovarian failure occurred in all patients and usually preceded the neurological symptoms. Neuroimaging shows bilateral confluent leukoencephalopathy and periventricular cystic degeneration. For patients presenting with POI with neurological signs the MRI and screening of the EIF2B mutations is indicated.
PYRAMIDAL PATHWAY CHANGES AT CONVENTIONAL BRAIN 3T-MRI IN PATIENTS WITH HEREDITARY SPASTIC PARAPLEGIA

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Background and Aims:: Conventional MRI can identify abnormalities associated with upper motor neuron (UMN) involvement. Motor cortex (MC) and cortico-spinal tract (CST) imaging abnormalities are reported in patients with amyotrophic lateral sclerosis (ALS), but their prevalence in other disease with UMN involvement is poorly studied. Our aim was to evaluate the occurrence of such changes in patients with hereditary spastic paraplegia (HSP).

Methods:: We retrospectively evaluated 3T-MRI from 44 HSP (27 men, mean age 49.3 ± 14.6), 55 ALS patients (35 men, 56.3 ± 7.6) and 52 controls (34 men, 53.4 ± 5.1). Features of interest were CCS T2/FLAIR hyperintensity, MC SWI hypointensity and selective MC atrophy. Differences among groups were tested using χ2 or ANOVA based on data (p < 0.05). We adjusted the analysis for age using logistic regression.

Results:: HSP patients had more frequently CCS FLAIR hyperintensity than controls but less than ALS patients (40.5%, 30% and 67.3% respectively; p<0.001). The prevalence of MC SWI hypointensity (HSP 69.2%, ALS 73.5%, controls 18.8%; p<0.001) and atrophy (HSP 73.8%, ALS 64.2%, controls 42.3%; p<0.01) was similar in HSP and ALS patients, both higher than in controls. The results did not changed adjusting for age.

Conclusions:: The prevalence of MC and CCS MRI abnormalities in HSP patients is higher than controls. However, it was similar to ALS patients, except for CCS FLAIR hyperintensity, less frequent in HSP, possible reflecting pathophysiological differences. The finding of such MRI features support a pyramidal involvement but is not able to discriminate between HSP and ALS.
VOLOTSKY INDEX IN PATIENTS WITH ISCHEMIC STROKE ACCORDING TO THE DERMATOGLYPHIC STUDY

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Background and Aims:: Aim is to determine and compare the Volotsky index and index range in patients with ischemic stroke and in healthy individuals using dermatoglyphic study.

Methods:: Fingerprints were taken from 52 patients with ischemic stroke and from 64 healthy individuals using the method of T.Gladkova. Dermatoglyphic analysis of the prints was carried out on the Papilone DC machine. Finger patterns-loops, arcs, curls, an the delta index are calculated. The Volotsky delta index is calculated using the formula: DL10 = (L+2W)/(A+L+W)*10, according to finger patterns A-L-W (arc-loop-curl).

Results:: In the group of patients, the index was 10.7%, and the index range was 8-18%, and in the group of healthy men, the index was 11.2%, the range was 6-16%; In women from the group of patients, the index was 14.5%, the range 9-20%; in women from the group of healthy individuals, the index was 10.6%, the range 6-16%; When determining the overall index in the group of patients, the index in male and female patients was 12.7%, and the range 8-20%. The overall index in the group of healthy individuals was 10.8%, and the range was 0-19%.

Conclusions:: In men from both groups Volotsky index and the range are similar. The index and the range are lower in healthy women than in women with ischemic stroke. Average value (in both men and women) of the index and the range are higher in the group of patients with ischemic stroke.
ADULT ONSET CEREBELLAR ATAXIA DUE TO NOVEL MUTATIONS IN BRAT1

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Background and Aims:: BRAT 1 (BRCA1-associated ATM activator 1) variants were first reported in 2012 in newborns with lethal neonatal rigidity and multifocal seizure syndrome (RMFS). They have also been associated with early onset neurodevelopmental disorder with cerebellar atrophy and with or without seizures (NEDCAS). More recently a milder phenotype characterized by nonprogressive cerebellar ataxia (NPCA) has been reported. We describe the case of a 66 year old woman with sporadic cerebellar ataxia, spasticity and mental retardation in whom we detected two novel mutations in BRAT1.

Methods:: NGS screening using targeted gene panels using a NextSeq Illumina platform was performed. The pathogenicity was investigated using Polyphen, SIFT and CADD score. The mutations were confirmed by Sanger sequencing.

Results:: The patient had started to complain gait disturbances with frequent falls since she was 55. She had also experienced rigidity, mild dysphagia and excessive sleepiness. Neurological examination showed ataxic gait, spasticity at four limbs, vertical gaze palsy, dysmetria and dysdiadochokinesia. Dysmorphic features as short stature, micrognathia and low set ears were also present. Extensive metabolic investigations were normal. EEG was normal. Brain MRI showed frontoparietal atrophy and cerebellar atrophy. Cognitive tests revealed mild cognitive impairment. Mutations in most common SCA loci were ruled out. Genetic analysis on NGS panels for genes associated with ataxia identified two novel compound heterozygous mutations in BRAT 1, c.605T>G (p.V202G) and c.333_346del (p.A112fs*74).

Conclusions:: Our case further expands the clinical spectrum of BRAT1 pathogenic variants suggesting to include BRAT1 gene in NGS panels screening for adult patients with cerebellar ataxias or spastic paraplegias.
CIDP ASSOCIATED WITH A NEW CONGENITAL MYASTHENIC SYNDROME: A CASE REPORT

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Background and Aims:: Congenital myasthenic syndromes (CMS) are a broad group of genetic-related neuromuscular transmission disorders. CIDP is an immune-mediated inflammatory disorder of peripheral nervous system. Both of these diseases are characterized by weakness, progressive in CIDP and often fluctuating in CMS. We report a case of CIDP associated with a new CMS subgroup

Methods:: A 27-year-old female patient was referred to our Institution with a diagnosis of CIDP. She was treated with intravenous immunoglobulins (IVIg) with marked benefits. When she was 33, during pregnancy, she complained ptosis, diplopia and marked weakness in both extensor digitorum muscles. Neurophysiological studies showed stable signs of CIDP, but these new symptoms did not respond to IVIg. So the patient underwent to repetitive nerve stimulation studies and single fibre EMG, which showed a neuromuscular transmission disorder. A repeated search for AChR and MuSK antibodies was always negative. No mediastinal alterations after CT scan were observed. Patient was diagnosed with seronegative myasthenia gravis. Pyridostigmine was not tolerated. Prednisone, azathioprine and mycophenolate treatments were ineffective and discontinued.

Results:: Due to the early onset of this neuromuscular transmission disorder a CMS was hypothesized and a genetic study was performed, showing a heterozygosis P506S in CHRNG gene, encoding gamma subunit in foetal AChR. This alteration had never been described so far and it is considered to be responsible for a slow-channel CMS.

Conclusions:: Foetal AChR is generally absent in adult neuromuscular junction: we hypothesized that the co-occurrence of CIDP may have triggered its expression, causing myasthenic signs development.
CHARCOT MARIE TOOTH DISEASE 2A, KIF1B PHENOTYPE; A CASE REPORT

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Background and Aims:: Background. Charcot Matie Tooth Disease (CMTD) has diverse inheritance patterns, affecting peripheric nerves through alterations in genes responsible for protein codification in Ranvier nodes. CMTD classification considers peripherical nerve velocity, inheritance pattern, among other factors; however, after the acknowledgment of multiple genes involved, a genetic classification should be considered. We present a case with an alteration in KIF1β.

Methods:: Case. 30-year-old female presenting axonal and demyelinating polyneuropathy (symmetric, sensory, and motor), multiple joint contractures, abnormalities in limb morphology, chronic skin erosions, vomiting crisis, and nausea. Alongside this, she presented cortical irritative activity, bilateral optic nerve atrophy, neurogenic bladder, and corpus callosum dysgenesis. She began with dermatological alterations at 6 years old. Variant in KIF1β was corroborated after a comprehensive diagnostic approach, suggesting CMT2A1.

Results:: Discussion. Alteration in MFN2 and KIF1β genes are classified in the same CMTD subgroup. Our patient presents phenotypic alterations not reported in other subgroups of CMTD. Case series of MFN2 disease coincide in the presence of axonal damage and optic atrophy. Although these were present in our case, KIF1β precipitates damage in other systems that constitute a phenotype not shared by subjects with MFN2 alterations.

Conclusions:: Conclusion. KIF1β alterations lead to a particular type of CMTD. This case shows the pathological presentation generated by its mutation and gives rise to considering the KIF1β CMTD subtype as an independent entity, suggesting the need for reclassification. We recommend the use of exome sequencing for mutations difficult to identify using previously available tools.
GENETIC MARKERS OF CATAMENIAL EPILEPSY IN WOMEN.

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**Background and Aims::** To study the role of the sodium channel gene (SCN1A) in the development of catamenial epilepsy.

**Methods::** Molecular genetic studies with determination of the frequency of alleles of the SCN1A gene were performed in 100 women examined by us. Of these, 60 patients with catamenial epilepsy, 20 with symptomatic epilepsy. The control group consisted of 20 healthy women of the same age. The alleles of the SCN1A gene of the polymorphic locus D2S2330 and D2S124 were studied.

**Results::** The frequency of occurrence of the alleles D2S2330*9, D2S2330*12 and D2S2330*11 was greater and reached from 10 to 15%, respectively. And we found the D2S2330*10 allele in only one patient with symptomatic epilepsy. In the control group, the alleles D2S2330*10 and D2S2330*12 were more common, which makes it possible to consider their presence as a criterion of reduced risk for catamenial epilepsy. The most common in the main group of patients were the D2S124*4 loci (28.3%) and D2S124*5 (21.6%), while the D2S124*5 locus in the control group was found in 10% of cases in the control group. Patients with DNA loci D2S214*2 (25%) and D2S214*3 (45%) were more common, while in the group of patients with catamenial epilepsy they were less common, locus D2S214*2-15% and locus D2S214*3-21.6%.

**Conclusions::** The relationship between the development of catamenial epilepsy and the SCN1A gene polymorphism at the D2S2330 and D2S214 loci was revealed, which does not exclude canalopathy in the pathogenesis of this type of epilepsy. This, in turn, plays an important role in the development of methods for predicting and differentiating therapy for catamenial epilepsy.
SEX-SPECIFIC DIFFERENCES IN TRANSCRIPTOMIC PROFILES AND CELLULAR CHARACTERISTICS OF OLIGODENDROCYTE PRECURSOR CELLS

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Background and Aims:: Oligodendrocyte precursor cells (OPCs) regulate the neuronal system in various ways and play crucial roles in brain homeostasis. Although recent studies have shown regional diversity and heterogeneity of OPCs, sex-related differences in OPCs are largely unknown. The purpose of present study was to investigate sex-specific differences in transcriptomic profiles and cellular characteristics of OPCs.

Methods:: For in vitro experiments, we prepared primary OPC culture obtained from neonatal rats. Sex identification was performed by PCR using sex-determining region Y gene. First, we evaluated the capacity of proliferation, migration, and differentiation in OPCs. Second, we examined the ischemic tolerance in OPCs after oxygen glucose deprivation. Third, we assessed the effects of OPC-derived factors on the integrity of blood brain barrier (BBB). For in vivo experiments, we conducted BrdU incorporation assay to assess the proliferation and differentiation of OPCs in adult mice. Finally, we performed RNA-seq analysis to investigate the sexual dimorphism in transcriptome profiles of cultured OPCs.

Results:: Female OPCs have a higher capacity for proliferation and migration. In addition, female OPCs are more resistant to ischemic stress, and can enhance the BBB integrity. Meanwhile, male OPCs have a higher capacity for differentiation and myelination. RNA-seq analysis revealed substantial transcriptomic differences in OPCs.

Conclusions:: The present study demonstrates sex-related differences in the cellular characteristics and transcriptional profiles of OPCs. Our findings may help to better understand the pathomechanisms of neurological and psychiatric diseases with sexual dimorphism.
EXPANDING THE DISEASE SPECTRUM OF RECESSIVE ECEL1 MUTATIONS BEYOND DISTAL ARTHROGYPOSIS PHENOTYPE

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Background and Aims:: Distal arthrogryposis type 5D (DA5D) is a rare autosomal recessive disorder with wide phenotypic spectrum. DA5D is caused by mutations in ECEL1.

Methods:: We describe two families (3 patients) with novel ECEL1 gene mutations detected by Next generation sequencing (NGS).

Results:: Patient 1: 12-year-old boy, born to consanguineous parents. He presented with birth asphyxia, motor developmental delay, severe contractures of fingers with webbing, pes planus, kyphoscoliosis, high arched palate, micrognatia, undeveloped testes, hypoplastic speech with nasal twang, asymptomatic ptosis, absent adductor digit minimi, bifacial and distal LL weakness. Muscle MRI revealed asymmetric fatty infiltration in gluteus maximus, rectus femoris, hamstrings and gastrocnemius. Patients 2,3: 17-year-old monozygotic twins born to consanguineous parents and presented with motor development delay, white hairlock, small low set ears, elbow and wrist contractures, hypotonia, thinning and weakness of all limbs (distal>proximal), pes cavus, areflexia with high steppage gait. One had perinatal insult, recurrent seizures, mental subnormality, nystagmus and primary optic atrophy. Electrophysiology revealed motor axonal neuropathy. MRI revealed extensive fatty infiltration of gluteus maximus, quadriceps, hamstrings, anterior and posterior compartment of leg. NGS revealed rare homozygous missense variants c.602T>C (p.Met201Thr) and c.83C>T (p.Ala28Val) in exon 2 of ECEL1 gene (Refseq: NM_004826.4). The variants were heterozygous in unaffected parents. In-silico predictions were damaging for both variants. While c.602T>C (p.Met201Thr) lies in the crucial Peptidase M13 domain with zero gnomAD frequency, c.83C>T (p.Ala28Val) is in proximal cytoplasmic domain with a minor allele frequency (MAF) of 0.006% in gnomAD.

Conclusions:: Our three cases expands the clinical and imaging spectrum of the ECEL1 mutations and associated DA5D.
A CASE OF 16 P11.2 DELETION WITH DELAYED DIAGNOSIS

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Background and Aims:: Chromosomal aberrations most commonly present with developmental delay and congenital malformation in childhood. Deletion 16 p11.2 is a rare chromosomal abnormality that leads to language dyspraxia, behavioural problems with autistic spectrum disorders and poor social skills, with less affection of global intellect. Epilepsy occurs in 20% of cases. Mild symptoms can lead to diagnostic delay

Methods:: Patient was reviewed in the adult neurology clinic. Case records and investigation results are summarised

Results:: A 32 years old lady presented to the neurology department with episodes of black outs that started during her first pregnancy. She had background of speech dyspraxia as a child, resolved by secondary school. She required support at school due to emotional and behavioural difficulties, attributed to social problems. The first episode was a collapse at work. Further episodes are brief periods of going blank, with no motor features or post ictal manifestations. EEG and MRI were normal. Lamotrigine led to reduced frequency of the episodes. 16 p11.2 deletion was detected as part of the workout for a son with developmental delay

Conclusions:: Developmental delay and behavioural changes can be caused by social, environmental or biological causes, such as genetic or metabolic disorders or perinatal insults. All patients, including mild and improving patients, should be worked out for potential underlying cause. Early diagnosis is important to provide appropriate support for patient and their families. Further studies are needed to define most cost-effective screening tests in milder cases.
Background and Aims:: Numerous studies have established that factors of the VEGFs (Vascular Endothelial Growth Factors) which are key regulators of angiogenesis, have a vasoactive effect and control the degree of vascularization of the vascular pathology.

Methods:: Objective studies were 188 patients with ischemic stroke. Of these, 105 with ischemic stroke associated metabolic syndrome with 3 or more components of MS (1 subgroup), 83 patients - with ischemic stroke on the background of relatively good somatic status, the presence of 1, 2 or the absence of components of the MS, (2 subgroup). The control group included 91 practical healthy people. Genomic typing was performed by methods based on the polymerase chain reaction.

Results:: Our study of the frequency of distribution of the alleles of the rs2010963 polymorphism of the VEGFA gene in groups of patients with stroke and control showed that the mutant allele “C” in the main group was statistically more frequent than in the control (the main group of patients was 27.1%; control - 13.7%; χ² = 10.18; p = 0.001; OR = 0.43; 95% CI (0.25-0.73)). The data obtained suggest the existence of an association between the carriage of the allele “C” of the rs2010963 polymorphism of the VEGF gene and the development of the stroke. The frequency of the allele “C” was significantly higher as in the subgroup of patients with stroke with no metabolic syndrome (subgroup B), (subgroup B - 28.13%; control - 13.74%; χ² = 8.56; p = 0.003 ; OR = 0.41; 95% CI 0.22–0.75), and patients with stroke with MS (subgroup A - 26.04%; control - 13.74%; χ² = 6.45; p = 0.01; OR = 0.45; 95% CI (0.24-0.84).

Conclusions:: In general, the data obtained indicate that the heterozygous genotype of the rs2010963 polymorphism of the VEGF gene makes a definite contribution to the development of the stroke, but is not associated with the metabolic syndrome.
CANNABINOIDS EFFICACY IN VANISHING WHITE MATTER DISEASE: A CASE REPORT.

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Background and Aims:: An oromucosal spray formulation (Sativex®) containing delta-9-
tetrahydrocannabinol and cannabidiol (THC-CBD) is indicated to treat unresponsive severe spasticity in
Multiple Sclerosis. A lot of clinical trials are underway demonstrating a potential role as supplemental
therapy in various neurological conditions, in particular addressing pain and spasticity in adults and
children.

Methods:: We present a 30-year-old man who was diagnosed with Vanishing White Matter Disease
(VWMD) at the age of 9. VWMD is a rare autosomal recessive syndrome characterized by progressive
white matter deterioration, due to mutations in either one of the five subunits of eukaryotic translation
initiation factor eIF2B. The classic phenotype includes ataxia, spasticity, cognitive decline and seizures
from early childhood. As young adult, our patient showed severe spastic tetraparesis with spasms and
neck muscle stiffness with right laterocollis.

Results:: Clonazepam, baclofen and botulinum injections were tried with poor results. THC-CBD spray,
at the dose of 8 sprays per day, improved muscular pain, spasms and night sleep, reduced modestly
spasticity and caused only mild drowsiness. To maximize the spasticity treatment, a baclofen intrathecal
infusion pump was positioned, but Sativex® was continued after surgery for its positive effect on patient’s
quality of life.

Conclusions:: To our knowledge, this is the first time that THC-CBD has been used in an adult patient
with VWMD. The treatment was well-tolerated and muscular spasm and night sleep improved as well as
the quality of life, despite the effect on spasticity was limited.
HEREDITARY LEUKODYSTROPHY WITH SPHEROIDS (HLDS) AND NASU-HAKOLA DISEASE (NHD): REPORTS OF SEVEN ITALIAN CASES TO HIGHLIGHT KEY DIAGNOSTIC FEATURES

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Background and Aims:: HLDS, an autosomal-dominant CSF1R-related leukoencephalopathy, and NHD, an autosomal-recessive TREM2- or TYROBP-related leukoencephalopathy, are ultra-rare adult-onset inherited microgliopathies. Based on their pathophysiology, hematopoietic stem cell transplantation (HSCT) might be a realistic therapy if performed at early stage. Aim of our work was to highlight diagnostic hints to promote prompt identification of affected subjects by reporting our experience.

Methods:: We reviewed data of four (1 male, 3 females) subjects with HLDS and three (two index cases) males with NHD assessed in the last 5 years in our Institute.

Results:: The diseases presented at a mean age of 43 (HLDS) and 31 (NHD) years with progressive cognitive-behavioral decline, often complicated by motor symptoms during the disease evolution. All the patients with the same diagnosis exhibit comparable neuro-images. Retrospectively, family history was positive in all HLDS cases and a possible founder effect was hypothesized for NHD based on identical genotype and geographical origin. Notably, all the patients were diagnosed late in the disease course.

Conclusions:: HLDS and NHD should be always considered in patients with progressive cognitive-behavioral decline and leukoencephalopathy. Specifically, predominantly anterior and asymmetric T2/FLAIR white matter (WM) hyperintensities with corpus callosum involvement are suggestive of HLDS, while diffuse atrophy with mild T2/FLAIR WM hyperintensity and basal ganglia micro-calcifications are suggestive of NHD. Provided the potential HSCT therapeutic efficacy, a diagnostic delay should be avoided, and a hub-and-spoke network among neurological and HSCT centers should be implemented for early diagnosis, familial counseling, HSCT eligibility assessment and structured follow-up.
A NOVEL DNM2 MUTATION IN A CASE WITH A PURE SENSORY AXONAL POLYNEUROPATHY

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Background and Aims: Dynamin 2, encoded by DNM2 gene, belongs to a family of pleiotropic GTPases. DNM2 gene mutations have been associated with several neuromuscular disorders, such as intermediate and axonal forms of Charcot-Marie-Tooth (CMT) disease. In this report, we describe clinical, instrumental and genetic aspects of a 59-year-old male patient carrying a novel DNM2 mutation and exhibiting a distinct phenotype of pure sensory axonal polyneuropathy.

Methods: We describe a case of a 59-year-old male with familial history positive for gait disorders. He presented an insidious onset of numbness and burning pain in the lower limbs. In addition, he had been suffering from obstinate constipation with intestinal obstruction. Neurological examination showed a “stomping” gait, reduced patellar reflexes, lower limbs global hypoesthesia with stocking distribution. Nerve conduction study revealed an axonal damage. Considering the overall clinical picture and the positive familial history, we performed a comprehensive molecular analysis of the genes responsible for hereditary neuropathies.

Results: The molecular analysis of the genes responsible for hereditary neuropathies, by means of Next Generation Sequencing approach, showed a novel p.Hys128Arg-DNM2 heterozygous mutation.

Conclusions: We described clinical, instrumental and genetic aspects in a patient affected by pure sensory axonal polyneuropathy and carrying the novel p.Hys128Arg-DNM2 heterozygous mutation, which further expands the spectrum of DNM2 mutations and related phenotypes. Another interesting feature we observed is subtle constipation, possible expression of gastro-intestinal autonomic dysfunction.
BETHLEM MYOPATHY TYPE 1 CAUSED BY A NEW MUTATION IN COL6A1GENE IN AN ALBANIAN PATIENT

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Background and Aims:: Bethlem myopathy represents the milder form of the spectrum of Collagen VI myopathies which are characterized by a clinical continuum with Ullrich congenital muscular dystrophy and Bethlem myopathy at each end of the spectrum, and less well-defined intermediate phenotypes between them. Bethlem myopathy is mainly an autosomal dominant disorder and the causing mutations occur in the COL6A1, COL6A2 and COL6A3 genes.

Methods:: We describe a case of a 12 year old male patient, the first Albanian case of Bethlem myopathy type 1. His symptoms begun in early childhood, with mild muscle weakness leading to delayed motor milestones. Symptoms progressed slowly, revealed mild proximal muscle weakness, lumbar hyperlordosis, protuberant abdomen, Achilles tendon retractions and a slightly myopathic gait. Gowers' sign was positive and laboratory testing revealed elevated creatine kinase value. Electromyography identified myopathic features with normal nerve conduction studies and muscle biopsy showed a myopathic pattern. Respiratory and cardiac function did not revealed significant changes.

Results:: Whole exome sequencing performed on the DNA of the patient and his parents identified a heterozygous likely pathogenic variant c.956A > G (Lys319Arg) in COL6A1 gene of the patient that explained the clinical phenotype. This mutation occurred de novo, since it was absent in the clinically unaffected parents.

Conclusions:: To our best knowledge, this is the first case report of Bethlem myopathy type 1 caused by a mutation in COL6A1gene in Albania. The molecular analysis provide the basis for the early diagnosis and proper management of these patients and expands genetic heterogeneity of the disease.
CASE REPORT: ROLE OF SCN9A THE SODIUM CHANNEL IN GENETIC EPILEPSY

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Background and Aims:: Childhood seizures are a frequent cause of pediatric emergency service admission. Genetic epilepsy is commonly related to multiple gene alterations. We report a case of childhood epilepsy associated with alteration in the sodium channel SCN9A gene sequence.

Methods:: Literature review was performed on the PUBMED, ScienceDirect and SCOPUS electronical database using the keywords: SCN9A gene mutation, CLDN16 mutation. All types of study design were taken into account, prioritizing those written in English or Spanish language and those using our keywords.

Results:: Mutations in the SCN9A gene were connected firmly with fever associated seizures or epilepsy with febrile seizures +, and that autosomal dominant patronus was the most common inherited pattern. However, Mutations, in γ-aminobutyric acid A receptor , commonly called GABA, and in sodium channels genes, which is the case of GABRG2, have been noticed to be related with febrile seizures and genetic epilepsy with febrile seizures +. In the case of the young female patient, there was a probably pathogenic variant, in the CLDN16 gene sequence, related to hypomagnesemia, additionally a pathogenic haplotype in the SCN9A gene sequence, in association with small fiber neuropathy. Both with an autosomal recessive inheritance pattern. The Clinic was mainly characterized by generalized tonic-clonic seizures, absences-type episodes and were exacerbated with emotions of anxiety and euphoria, obsession with certain activities such as ordering clothespins by color and playing all the time a single game.

Conclusions:: Child seizures represent a diverse set of medical conditions. The clinical course of the disease, response to treatment is significantly different.
NEURO-ENCEPHALIC FEATURES OF TUBEROUS SCLEROSIS COMPLEX

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Background and Aims:: Tuberous sclerosis is a phacomatosis resulting from an autosomal dominant inheritance. It is characterized by the presence of multiple hamartomas in various organs, especially the brain, the skin, the kidneys and the heart. The aims of this study is to focus on neuro-encephalic features of tuberous sclerosis complex.

Methods:: The authors report personal cases series and review the literature highlighting epidemiology, clinical features and imaging of neuro-encephalic tuberous sclerosis.

Results:: The diagnosis of tuberous sclerosis is based on imaging and clinical examination, where magnetic resonance imaging constitutes the key investigation showing characteristic brain lesions.

Conclusions:: Neuro-encephalic manifestations may be particularly severe, and may even be life threatening. the advances in the field of genetics offer the possibility of a new avenue of research in the management of tuberous sclerosis based, on the one hand, on the inactivation of mTOR, and, on the other hand, on the factors acting on the TSC1 – TSC2 interaction.
EXPRESSION PROFILING OF CIRCULATING MIRNA IN THE NEUROFIBROMATOSIS TYPE 1 AND RELATED CANCERS IN A LARGE NF1 ITALIAN COHORT

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Background and Aims:: MiRNAs are short noncoding RNAs involved in regulating gene expression at post-transcriptional level. Several studies have suggested their role as biomarkers for various diseases. Its roles in mediating tumorigenesis remain largely unexplored in many disorders, including Neurofibromatosis type 1 (NF1, OMIM#162200), the most frequent autosomal dominant tumour predisposition syndrome, caused by loss-of-function mutations in the NF1 gene. The study aims to identify circulating miRNA profiling in the NF1 and NF1-related cancers and deregulated miRNA gene-target pathways associated to different NF1 phenotypes.

Methods:: The study includes familial/sporadic NF1 patients, enrolled at Division of Neurology of AOU Luigi Vanvitelli and diagnosed based on the NIH Consensus Conference criteria of 1988. According to clinical characteristics, different subgroups have been classified: NF1 without systemic complications (Group 1), NF1 with systemic complications (Group 2), NF1-MPNST (Group 3), NF1 with neurological malignancies (Group 4), NF1 associated to other organ tumours (Group 5). For each clinical groups and controls 15 serum samples were pooled and RNA was extracted and analyzed through NGS. Deregulated miRNAs were studied to identify their specific target genes and related molecular pathways.

Results:: Differential miRNA signatures were identified in each NF1 clinical groups. Deregulated miRNAs identified in this study are involved in the tumorigenesis, cell cycle, cell proliferation, DNA damage, necrosis, apoptosis and angiogenesis processes.

Conclusions:: NF1 is characterized by a highly inter- and intrafamilial clinical variability. The identification of circulating miRNA profile is essential for an early NF1 diagnosis and to distinguish between different disease phenotypes.
NEUROFIBROMATOSIS TYPE 1: MOLECULAR SPECTRUM OF THE NF1 MUTATIONS IN A LARGE COHORT OF ADULT ITALIAN PATIENTS

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Background and Aims:: Neurofibromatosis type I (NF1, OMIM #162200) is one of the most common genetic tumor predisposition syndrome, caused by loss of function mutations in the NF1 gene. To date, no clear genotype-phenotype correlation has been discerned in NF1. We aimed to investigate the molecular spectrum of NF1 gene and evaluated the genotype-phenotype correlations in a large cohort of adult Italian NF1 patients.

Methods:: Our series includes 85 familial/sporadic NF1 patients, enrolled at Division of Neurology, Neurofibromatosis and Rare Diseases Center of AOU Luigi Vanvitelli. The clinical data were collected at the time of mutation analysis and re-verified for accuracy at the time of this study. Blood samples were collected for molecular NF1 genetic testing and informed consent was obtained in all patients. A combination of targeted next-generation sequencing and multiplex ligation-dependent probe amplification was performed for molecular analysis.

Results:: We identified 69 different NF1 mutations, including missense, nonsense, start loss, frameshift and splicing mutations, distributed along the entire gene. Multi-exons duplications/deletions and deletion of the entire NF1 gene were also identified. In our cohort, nonsense and splicing affected mutations were mainly detected in NF1 patients showed skeletal complications, while frameshift mutations could be associated to learning impairment in NF1 female patients.

Conclusions:: This study led to the identification of novel NF1 mutations and offered an important contribution to the genotype-phenotype studies in the NF1 pathogenesis.
FAHR’S SYNDROME ASSOCIATED WITH HEREDITARY ANGIOEDEMA: A CASE REPORT

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Background and Aims:: Fahr’s syndrome is defined by the presence of bilateral and symmetrical intracerebral calcifications, nonarteriosclerotic, localised to the basal ganglia. Hereditary angioedema associated with Fahr’s syndrome is unheard of.

Methods:: we report a case report of hereditary angioedema associated with a Fahr’s syndrome.

Results:: the observation of a 28-year-old patient from a consanguineous marriage, followed since the age of 7 for epilepsy under sodium valporoate, with discovery of a hereditary angioedema associated with a Fahr’s syndrome. Clinically, the patient presents with mental retardation, behavioral disturbances, soft and painless white facial edema with eyelid occlusion suggestive of angioedema. Laboratory assessment: hypocalcemia (33 mg / L), hyperphosphatemia (99 mg), hypoparathormonemia (10 IU), and hypovitaminosis-D (10 g / L). The inhibitory C1 level is less than 30% of the normal value, the serum C4 is less than 0.10, and the C3 is normal. Brain scan: bilateral and symmetrical calcifications of the two caudate, lenticular nuclei, the two thalami, and the dentate nuclei. Patient was put on replacement therapy (calcium 2 g / d + Un alfa 0.5ug × 2 / d + magnesium 300mg / d), exacyl 1500mg / d, in combination with neuropsychiatric treatment.

Conclusions:: The discovery of hereditary angioedema during Farh syndrome constitutes an exceptional association, and should lead to a study of the inhibitory C1 complement with assay of these C3 and C4 fractions.
LIPOTOXICITY ALTERS THE CHAPERONES AND SYNAPTIC FIDELITY VIA EPIGENETIC MODULATIONS IN MAMMALIAN DERIVED HIPPOCAMPAL CELLS

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Background and Aims:: Epigenetics are the inaudible signatures of several pathological processes in the brain. This study understands the influence of DNA methylation, a major epigenetic modification, in the lipotoxic hippocampal neurons and its notable effect on the cellular chaperones and synaptic proteins.

Methods:: The neurolipotoxicity was induced in HT22 hippocampal cells using LPS and sodium palmitate, a saturated fatty acid; and the DNA methyltransferase (DNMT) levels were measured to study the DNA methylation, a major epigenetic marker. The levels of cellular chaperones and synaptic proteins were examined using DNMT inhibitor, 5-aza-2′-deoxycytidine (5-aza-dC)-treated cells. Methylation analysis were also done to understand the hypo- or hyper-methylation of these proteins. Apart from it, the DNMT enzymes were docked with the synaptic proteins, to understand the protein-protein interactions a bit in detail, using the PIPER algorithm in the Schrodinger (bioinformatic tool) suite.

Results:: Altered DNA methylation were confirmed in the LPS and palmitate induce lipotoxic cells. Pretreatment with AzadC, ameliorated the protein and gene expression of cellular chaperones and synaptic proteins, concluding a link between the proteins and methylation. The insilico results showed a stable and preferred binding of these proteins within the active domain of the DNMT enzyme. Methylation analysis in the promoter region of these proteins further justified the epigenetic involvement in the lipotoxic hippocampal cells.

Conclusions:: Lipotoxic damage to the hippocampal cells, were rescued by demethylation treatment, and also accorded in improving the memory-associated proteins, suggesting a substantial contribution to the underlying pathophysiology of several metabolic syndromes linked with the cognitive abilities.
MODERATE PHENOTYPE OF A CONGENITAL MYASTHENIC SYNDROME TYPE 19 IN AN ALGERIAN PATIENT.

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Background and Aims:: Congenital myasthenic syndromes (CMS) represent phenotypically and genotypically very heterogeneous conditions. No less than 32 genes have been identified to date. CMS caused by mutations in the COL13A1 gene are very rare and have a phenotype described as severe. We present the first case of CMS described in Algeria and the Maghreb with a mutation of this gene.

Methods:: Our patient underwent a complete neurological examination with myasthenic score, electromyographic examination and DNA sampling for a genetic study.

Results:: Our patient presenting a rather moderate phenotype with bilateral ptosis, fluctuating during the day and evolving from birth. Neonatal hypotonia is not noted, nor any delay in motor acquisitions. During the investigation of this patient, and despite the very probable congenital origin, we ruled out other diagnoses which could induce pathology of the neuromuscular junction (NMJ). The genetic study confirmed our diagnostic suspicion by highlighting a new mutation in the COL13A1 gene.

Conclusions:: This is the first mutation of this gene found in the Maghreb and which demonstrates that its phenotype can be moderate, contrary to what is reported in most of the cases reported to date.
ASSOCIATION OF DEPRESSION WITH POLYMORPHIC MARKER VAL158MET OF COMT GENE IN AN OPEN POPULATION 25-44 YEARS: EPIDEMIOLOGICAL STUDY

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Background and Aims:: We aimed to study the association of polymorphic marker Val158Met COMT gene regulating the concentration of extracellular dopamine with depression in an open population of 25-44 years.

Methods:: A representative sample of the population in Novosibirsk of 25-44 years of age was examined in 2013-2016 (n=975, 43.8% males, mean age 34.5±0.4 years) in frame of budgetary theme # AAAA-A17-117112850280-2. Levels of depression assessed by means of the "MONICA-psychosocial" scale. A cohort of 441 persons (50.8% males) underwent genotyping for Val158Met (rs4680) polymorphism of the COMT gene.

Results:: In the open population of 25-44 years of age the prevalence of major depression (MD) was 13.2%, the average level was 24.4%. Persons with G/G genotype of the COMT gene were more likely to have MD. It was found in 61.8% compared to those with the A/A genotype (38.2%) (χ²=6.097 df=2, p=0.047); also the carriers of G allele (55.3%) had MD more often than carriers of A allele (44.7%) (5.408 df=1; p=0.02). Among male carriers of the A/A genotype of the COMT gene, MD was less common (15.8%) than among carriers of the G/A genotype (84.2%) (χ²=4.603 df=1; p=0.032). Female carriers of G/G genotype had MD more often (65.5%) than carriers of A/A genotype (34.5) (χ²=4.769 df=1; p=0.029). G allele (58.2%) was more common among women with MD than A allele (41.8%) (6.658 df=2; p=0.01).

Conclusions:: Based on the received data we can assume that the G/G polymorphic marker of the COMT gene may be associated with high levels of depression.
THE ROLE OF THE NEUROLOGIST IN THE DIAGNOSTIC ROUTE OF HSP AND CEREBELLAR ATAXIAS IN THE NEXT GENERATION SEQUENCING ERA: A SINGLE CENTER EXPERIENCE

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Background and Aims: The molecular characterization of Hereditary Spastic Paraplegias (HSP) and inherited cerebellar ataxias (CA) is challenged by their clinical and molecular heterogeneity. The recent application of NGS technologies is increasing the diagnostic rate, which can be also influenced by patients’ selection.

Methods: To assess how a clinical diagnosis of CA/HSP received in a third-level reference center might impact on the molecular diagnostic yield, we retrospectively evaluated the molecular diagnostic rate reached in 192 unrelated families (90 HSP and 102 CA) i) before NGS ii) by the use of NGS gene panels.

Results: Overall, 46.3% families received a genetic diagnosis by first-tier individual gene screening: 43.3% HSP and 50% SCA. The diagnostic rate was 56.7% in AD-HSP, 55.5% in AR-HSP, and 21.2% in sporadic HSP. On the other hand, 75% AD-, 52% AR- and 33% sporadic CA were diagnosed. 32 patients (24 CA and 8 HSP) were assessed by NGS gene panels, and 34.4% were diagnosed, including 29.2% CA and 50% HSP patients. 11 novel gene variants classified as (likely) pathogenic were identified.

Conclusions: Compared with literature data, our results support the critical role of experienced clinicians in the diagnostic assessment and the clinical research of CA and HSP even in the next generation “era”.
Background and Aims:: Hereditary Spastic Paraplegias (HSPs) are characterized by progressive spasticity and weakness of lower limbs and comprise of ‘pure’ and ‘complicated’ phenotypes. HSPs are genetically diverse and data from India are limited. We aimed to comprehensively analyze the genetic basis in a large cohort of HSP from India and correlate with the phenotype.

Methods:: Patients with HSP phenotype from a single neurology unit were evaluated for their clinical features, electrophysiological and radiological abnormalities. Genetic analyses were carried out by clinical exome sequencing (n=52) and targeted sequencing (n=5).

Results:: The cohort comprised 40 men and 17 women. The age ranged from 3.5 to 49 years. There were 25 children (age<=18 years). All patients presented with insidious onset, progressive difficulty in walking and bilateral pyramidal signs. Based on the clinical features, 15 (26.3%) patients were classified as ‘pure’ and the remaining 42 (73.7%) as ‘complicated’ forms of HSP. Brain MRI showed thin corpus callosum (n=10), periventricular hyperintensities (n=20), cerebral atrophy (n=3), cerebellar atrophy (n=3) and diffuse atrophy (n=4). Sixty-seven variants representing 40 genes were identified including 47 novel variants. Forty-eight patients (84.2%) had variants in genes previously implicated in HSP and other spastic paraplegia syndromes (SPG genes=24, non-SPG genes=24), among these 13 had variations in more than one gene.

Conclusions:: The current study led to the identification of the spectrum of genetic variations in a large cohort of comprehensively evaluated patients with HSP phenotype from India. Our cohort was characterized by a wide age range, male predominance, and increased representation of sporadic and ‘complicated’ HSPs.
GENOMIC ANALYSIS IDENTIFY A NEW EIF2B3 GENE VARIANT DETECTED IN AN UNCERTAIN CASE OF CADASIL DISEASE

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Background and Aims:: Vanishing white matter disease (VWM) is an autosomal recessive leukodystrophy caused by mutations genes encoding the translational initiation factor 2B: EIF2B1-EIFB5. It is a heterogeneous neurological disorder with prominent cerebellar ataxia and spasticity in childhood-onset form and behavioural changes, dementia and seizures in adult-onset form (15% of cases). We present the case of a 60 years old patient, MTHFR homozygous, presenting white matter lesions and a subcortical vascular encephalopathy being diagnosed. To investigate a possible genetic cause, suspecting CADASIL, genetic and genomic analysis were performed.

Methods:: Sanger sequencing and Next Generation Sequencing (NGS) analysis were performed on the patient. NOTCH3 sequencing was performed using primer pairs for all 22 exons, for NGS analysis we used a genes panel including 753 genes involved in neurological diseases.

Results:: NGS detected a novel heterozygous non-synonymous variant in exon 5 of EIF2B3 gene (c. C554G; p. S185C), whose mutations have been strongly related to leukoencephalopathy and VWM disease. Furthermore, all in silico analysis conducted on this variant predicts its deleterious impact that could affect protein function.

Conclusions:: S185C variant in EIF2B3 gene was discovered in an atypical condition of adult onset Leukodistrophy, a disease that usually occurs in childhood. It is uncertain if S185C could be responsible for the clinical history of our patient or if the peculiarity of his symptoms could be related to the potential contribution of this new detected variant on the phenotypical spectrum observed in the disease.
AN INTERESTING CASE OF DIZZINESS: BOW HUNTER’S SYNDROME DUE TO KIMMERLE ANOMALY DIAGNOSED WITH PROVOCATIVE DSA

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Background and Aims:: BACKGROUND: Rotational occlusion of the vertebral artery known as Bow hunter’s syndrome (BHS) is a very rare cause for transient vertebrobasilar insufficiency symptoms. Complete or incomplete ossification of the posterior atlantooccipital membrane is called a Kimmerle anomaly which causes symptom in only 5.5% of patients with this anomaly. Early diagnosis with high index of clinical suspicion and provocative digital substraction angiography aids in prompt surgical repair, relieving the patient from the disabling symptoms and avoiding unnecessary ineffective symptomatic therapies. Objective: To report a rare case of 51-year-old driver who presented with transient giddiness who was on vestibular sedatives for long, having symptoms only on reversing his car in rightward head rotation diagnosed with provocative digital subtraction angiography (DSA).

Methods:: An interesting clinical history and unique advanced imaging findings with illustrative images are reported.

Results::
Provocative DSA revealed dynamic stenosis of left vertebral artery at C1 vertebral level. CT angiogram revealed ponticulus posticus or kimmerle anomaly occurring due to calcification of the posterior atlanto-occipital (PAO) membrane and treatments with surgical correction was advised. A high index of clinical suspicion helps in prompt diagnosis of BHS in patients with transient vertebrobasilar insufficiency.

**Conclusions:** This case highlights the importance of provocative DSA in making the definitive diagnosis of the rare Bow hunter's syndrome and also reports its causal association with calcified PAO membrane or Kimmerle anomaly which if managed early can improve symptoms significantly.
Background and Aims:: White matter hyperintensities on magnetic resonance imaging (MRI) are a frequent finding. Anaplastic astrocytoma as a cause of persistent, symmetrical white matter hyperintensities is unusual.

Methods:: A 22-year-old male presented with an episodic, non-specific headache for one month duration, which was followed by brief episodes of altered awareness and a progressive decrease in consciousness. The physical examination showed a reduced conscious state without any focal neurological signs. Non-contrast CT brain showed cerebral oedema and dilated temporal horns of the lateral ventricles. MRI-brain showed extensive, symmetrical T2 and FLAIR hyperintensities involving the corpus callosum, pericallosal region, periventricular white matter, deep white matter and bilateral cerebellar hemispheres surrounding the dentate nuclei, without diffusion restriction or contrast enhancement. In addition, the body of the lateral ventricles were compressed leading to dilatation of the temporal horns. The CSF full report was normal and the CSF cultures and cytology was negative. External ventricular drainage was placed after consultation with the neurosurgeons. He was treated with IV 3% sodium chloride for a few days and IV dexamethasone, IV ceftriaxone and IV aciclovir for 14 days. There was no significant clinical or radiological improvement. A ventricular wall biopsy was performed. This showed an anaplastic astrocytoma (WHO Grade 111). The patient was subsequently referred for specialized oncological management, but succumbed to his illness following the initiation of chemotherapy.

Results::
GFAP immunostain

**Conclusions:** This case highlights the unusual presentation of a primary CNS tumour with symmetrical, persistent white matter hyperintensities.
Background and Aims:: Neuromyelitis optica (NMO) is characterized by acute transverse myelitis and bilateral or rapidly sequential optic neuritis. The diagnosis is based on clinical, imaging and laboratory data. We describe a case where transorbital sonography (TOS) shows a promising role in performing diagnosis and monitoring clinical course, when combined with strict clinical follow up.

Methods:: A 23-year-old woman complained of acute visual loss in left eye associated with pain and loss of color vision; ophthalmic examination revealed a papillitis. Visual evoked potential showed unilateral prolongation of P100 latency. TOS revealed increased optic nerve sheath diameter (ONSD). She was treated with intravenous prednisolone with rapid recovery. Four months later, she experienced an identical episode of visual loss in the left eye.

Results:: Extensive laboratory work-up, including viral, toxic, metabolic and vasculitis screening and cerebrospinal fluid analysis, was unremarkable. IgG Aquaporin-4 (AQP) serum antibody test was positive. MRI revealed a longitudinal syringomyelia cavity extending T7-T10, without brain abnormalities. According to the international diagnostic criteria, a diagnosis of NMO was made. At TOS, initially, an enlargement of ONSD on the left side was found, that subsequently decreased up to normalization; at subsequent control at 120 days, when the patient experienced a relapse of optic neuritis, both unilateral ONSD enlargement and optic disc elevation were observed, that later normalized after that immunomodulatory therapy was started.

Conclusions:: Seriated TOS monitoring was a useful predictor of clinical course of recurrent papillitis in neuromyelitis optica. Further studies are needed to demonstrate accuracy of TOS respect to visual evoked potentials and retinal imaging.
FUNCTIONAL CONNECTIVITY AS AN EARLY MARKER FOR DEEP BRAIN STIMULATION IN PARKINSON’S DISEASE

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Background and Aims:: To identify functional neuroimaging patterns anticipating the clinical indication for DBS in PD.

Methods:: PD patients underwent clinical and cognitive evaluations and resting-state fMRI (RS-fMRI) at baseline and every year for a maximum of four years. Patients were divided into two groups: 19 patients eligible for DBS (PD-DBS) over the follow-up and 41 patients who did not meet the criteria to undergo DBS (PD-noDBS). Sixty age- and sex-matched healthy controls performed baseline evaluations. Graph analysis and connectomics assessed global and local topological network properties and regional functional connectivity at baseline and at each time point.

Results:: Network analysis showed a higher mean nodal strength, local efficiency and clustering coefficient of the occipital areas in PD-DBS relative to both controls and PD-noDBS at baseline. The occipital hyperconnectivity pattern was confirmed also by regional functional connectivity analysis. On the contrary, a significantly decreased functional connectivity between basal ganglia and sensorimotor/frontal networks was found in PD-DBS compared to PD-noDBS patients at baseline. In the longitudinal analysis, PD-DBS patients showed a progressive decreased topological brain organization and functional connectivity, mainly in the posterior brain networks, and a progressively increased connectivity of basal ganglia network compared to PD-noDBS patients. Baseline occipital hyperconnectivity in PD-DBS patients was related to tremor severity at baseline and over time.

Conclusions:: RS-fMRI may support the clinical indication to DBS and could also be useful in predicting which patients would be eligible to undergo DBS in the earlier stages of PD. Funding: Ministry of Education, Science, and Technological Development, Republic of Serbia (#175090)
Background and Aims:: Brain structures other than basal ganglia are likely to be involved in the pathophysiological process of Parkinson’s disease (PD). The role of cerebellum in PD has been explored during motor tasks involving the hand, while few studies investigated its activity during gait-simulating tasks and dual-task situations. This study aimed at assessing structural and task-based functional cerebellar alterations in PD patients with postural instability and gait disorders (PD-PIGD).

Methods:: Twenty-one PD-PIGD patients and 23 age and sex-matched healthy controls underwent clinical, structural and functional MRI, including a motor-task (foot anti-phase movements) and a dual-task (foot anti-phase movements while counting backwards by threes). Regional grey matter cerebellar volumes were assessed automatically using an atlas propagation and label fusion strategy based on the freely available human cerebellum template and probabilistic atlas (SUIT). FMRI images were co-registered with structural images and cerebellar fMRI analysis was performed.

Results:: PD-PIGD patients showed reduced volumes in several cerebellar motor and non-motor areas relative to controls. During both fMRI motor-task and dual-task, patients showed greater activation of cognitive cerebellar areas (crus 1-2) relative to healthy subjects and a reduced activity of motor areas (lobules I-IV and VIIIb).

Conclusions:: The increased activity of non-motor cerebellar areas might be a consequence of grey matter atrophy or an attempt to compensate the functional failure of cerebellar motor areas. Structural and functional MRI metrics focusing on cerebellum are useful to characterize brain correlates of motor and dual-task abilities in PD-PIGD patients.
BIANCA-MS: A NOVEL ARTIFICIAL INTELLIGENCE TOOL FOR MULTIPLE SCLEROSIS AUTOMATED LESIONS SEGMENTATION

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Background and Aims:: Automated white matter lesions segmentation in multiple sclerosis (MS) is still an open field and no standardized approach has been widely employed yet. We aim to validate BIANCA-MS, a novel tool for MS lesions segmentation on brain MRI, based on the original version of BIANCA (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki) and which implemented: i) a harmonized setting tested under different conditions, avoiding the need to further tune algorithm parameters to each dataset; ii) a post-processing cleaning step to refine lesion segmentation.

Methods:: 470 scans at 1.5 and 3T from three different datasets were analysed. For each scan, manually outlined masks were provided. We first tested algorithm behaviour across different scanning conditions. Further, on datasets where FLAIR images (2-3D) were provided, we compared BIANCA-MS to lesion prediction algorithm (LPA), lesion growth algorithm (LGA) and nicMSlesions. Performances were evaluated in comparison to manual segmentation using spatial similarity index (SI) and the number of false positive/negative clusters (nFPC/nFNC).

Results:: BIANCA-MS provided consistent results across datasets for SI, irrespective of the scanning protocol. The third datasets showed higher nFPC and nFNC (table 1, p<0.01). BIANCA-MS showed higher SI (table 2, p< 0.01) and higher sensitivity (lower nFNC, p<0.01) than LPA, LGA and nicMSlesions. However, BIANCA-MS showed less specificity (higher nFPC, p<0.01) than LGA and nicMSlesions.

Conclusions:: The comparable performances achieved across datasets proved BIANCA-MS robustness.
and flexibility. Further, our pipeline avoided the long optimization procedure needed to tune algorithm parameters. Finally, compared to other tools, our approach showed higher degree of similarity to manual segmentation.
ATROPHY QUANTIFICATION IN MULTIPLE SCLEROSIS: APPLICATION TO THE MULTICENTER INNI DATASET

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Background and Aims:: Aim of this study was to compare a set of methods for gray matter (GM) and whole-brain atrophy measurements on the Italian Neuroimaging Network Initiative (INNI) dataset, where MRI and clinical data from multiple sclerosis (MS) patients and healthy controls (HC) are collected by Italian Research Centers with recognized expertise.

Methods:: SIENAX, SPM v12 and Jim8 (Xinapse-Systems) software were selected. 3D MPRAGE from 457 MS and 271 HC were collected from INNI repository. For cross-sectional GM and whole-brain atrophy measures, we evaluated the agreement and correlation among the results of the pipelines. Moreover, the capability of the software in discriminating between HC and MS was assessed. A bias due to the different acquisition Center and the sample size requirement were also evaluated.

Results:: We found significant agreement (p<0.05) among the software: the highest between the results of SPM and Jim8 (0.91, p<0.05) and the lowest between SIENAX and Jim8 (0.6, p<0.05), for both GM and whole-brain. Comparing distributions, SIENAX for GM and Jim8 for brain volumes better separated HC from MS (p<0.05). None of the pipeline showed a bias in respect to a particular Center.

Conclusions:: We found acceptable agreement among the software. The free-licence (SIENAX), the speed and the facility of integration in the clinical routine (Jim8, SIENAX) are noteworthy for the selection of the atrophy pipeline. To move those atrophy tools from the research setting to the clinical practice, normative data from at least 150 HC should be available. Funding. This study was partially supported by Fondazione Italiana Sclerosi Multipla (Grant n.FISM2019/S/3).
Background and Aims:: We assessed white matter (WM) atrophy in multiple sclerosis (MS) both cross-sectionally and longitudinally with advanced DWI-techniques and explored whether these measures would better explain clinical and cognitive outcomes in comparison with conventionally used metrics.

Methods:: Baseline and one-year clinical evaluation, 3DT1-weighted and DWI sequences were obtained from 86 MS patients and 55 healthy controls (HC). Maps of fractional anisotropy and mean diffusivity were derived from DWI; intra-cellular volume (v_{IC}) maps were computed from neurite orientation dispersion and density imaging model. A fixel-based morphometry analysis was applied to estimate voxel-wise fiber-bundle cross-section (FC) atrophy in MS compared to HC.

Results:: Only FC measure showed a significant atrophy in relapsing-remitting (RR) MS compared to HC and in progressive patients compared to RRMS, mainly located in the cortico-spinal tract, splenium of the corpus callosum, optic-radiation and cingulum (p-value<0.05), both at baseline and after one year. Globally at baseline, FC and v_{IC} were significantly associated with the Expanded Disability Status Scale (r=-0.3) and the Symbol Digit Memory Test (r=0.39) respectively, being the selected predictors of clinical (R-sq=0.33, p=0.007) and cognitive scores (R-sq=0.29, p=0.0014) in a linear regression model.

Conclusions:: By identifying tract-specific differences, voxel-based analyses confirmed the ability of FC measure to detect WM atrophy with greater anatomical specificity compared to other measures and better capability to distinguish MS clinical phenotypes and their longitudinal WM degeneration. FC and v_{IC} were the best predictors of clinical disability and cognitive scores at baseline. Funding: This study was partially supported by Fondazione Italiana Sclerosi Multipla (Grant 2018/R/16).
CORTICAL REMODELING ACROSS THE LIFESPAN IN HEALTHY BRAIN REVEALS STRUCTURAL NETWORK VULNERABILITY TO NEURODEGENERATION

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Background and Aims:: Aging is the main risk factor for most of the neurodegenerative diseases. The aim of this study was to investigate cortical thinning changes across lifespan in healthy brain revealing structural network vulnerability to neurodegeneration.

Methods:: The cohort included 128 healthy individuals aged 20-85 years, who underwent an MRI scan. T1-weighted images were used to estimate vertex-wise cortical thickness maps, then grouped into 83 regions. For each region, cortical thickness trajectory with advancing age was estimated, including sex as covariate. Regions were ranked based on their relative thickness at the end of the observed lifetime, assessing regional changes over time. Mean regional thickness was correlated with relative change over time.

Results:: The highest cortical thinning was observed in the temporal lobe (parahippocampal, entorhinal, superior and middle temporal, and fusiform), frontal lobe (lateral orbitofrontal, superior and inferior frontal, including pars triangularis and opercularis, and rostral anterior cingulate), parietal lobe (the isthmus of cingulate, precuneus, supramarginal and inferior parietal) and in the insular cortex. Interestingly, occipital regions (cuneus, lateral occipital, lingual, pericalcarine), and motor and premotor areas (precentral, postcentral and paracentral regions) showed the least cortical thickness change compared to the whole brain across lifespan. Finally, positive correlation was found between mean regional thickness and its relative change over time.

Conclusions:: This study highlights structural vulnerability of brain regions to aging and provides information concerning trajectories of normal brain aging, identifying those areas that might be more vulnerable to the attack of neurodegeneration. Funding: European Research Council (StG-2016_714388_NeuroTRACK).
NEUROIMAGING IMPROVES THE PREDICTION OF POST-STROKE MAJOR NEUROCOGNITIVE DISORDER

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Background and Aims:: Neurocognitive disorder (NCD) appears in 10% of survivors of a first-ever stroke and in 30% after a recurrent one. We aimed to classify clinical and imaging factors related to major NCD 3 months after stroke, so as to find the optimal composition of factors for prediction of rapid development of the disease.

Methods:: 227 stroke survivors (age = 71.7 (11.3), NIHSS = 3.8 (4.8), females = 43.6%) were included from the ‘Norwegian COgnitive Impairment After STroke’ study. Clinical- and MRI data at baseline, and neuropsychological data at baseline and 3 months was used. The imaging factors included cortical thicknesses (automatically measured using Freesurfer), white matter hyperintensity volumes (semi-automatically measured using FSL Bianca), and stroke lesion volumes (semi-automatically measured using ITK-snap). Support Vector Machine classification was used in order to investigate the prognostic value of the factors. Model performance was measured using Area Under Receiving Operating Characteristics (ROC) and -Curve (AUC).

Results:: The model containing clinical factors only was driven by 12 of 14 variables and achieved an AUC of .790. The model containing both clinical and imaging factors was driven by 19 of 26 factors and achieved an AUC of .876.

Conclusions:: The model containing both the clinical and the imaging factors was able to predict rapid onset of major NCD with a higher accuracy than did the model with only clinical factors, demonstrating the importance of including imaging findings in rapid onset post-stroke NCD prediction.
POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES) AS A COMPLICATION OF PURULENT MENINGITIS: CASE REPORT AND REVIEW OF THE LITERATURE.

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Background and Aims:: Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological syndrome characterized by subcortical parieto-occipital vasogenic edema. Pathophysiology is not fully understood but endothelial injury and disregulation of vascular autoregulation seem to play a key role. We describe the case of a patient diagnosed with meningitis complicated by PRES and intracranial hemorrhage.

Methods:: A 71-year-old woman presented to the emergency department with impaired level of consciousness, headache, photophobia and hypertension (185/85 mmHg). Brain CT and CTA were normal. Shortly after admission fever appeared and alertness worsened further. Clinical examination revealed nuchal rigidity and a positive Kerning’s sign. Cerebrospinal fluid (CSF) analysis revealed pleocytosis and elevated protein leading to a diagnosis of bacterial meningitis. Despite thorough investigation no pathogen was identified. Empirical broad-spectrum antibiotic treatment was started. Brain MRI showed a necrotic-hemorrhagic lesion in left posterior parietal-occipital lobe with bilateral posterior white matter edema, consistent with PRES. After one week, repeated MRI and CSF analysis showed a significant reduction of white matter edema and pleocytosis. The patient fully recovered except for right homonymous hemianopia.

Results:: Severe infection is a known cause of endothelial damage which can lead to failure of cerebral vessel autoregulation and PRES. The exact occurrence of this correlation may be underestimated. PRES has a generally favorable prognosis but patients may develop severe complications among which intracranial hemorrhage.

Conclusions:: PRES is a neurologic syndrome characterized by typical imaging findings and associated with a wide variety of comorbidities, including severe infections. Early recognition of underlying conditions and appropriate treatment are fundamental to revert parenchymal involvement.
CONVERGING LONGITUDINAL PATTERNS OF ATROPHY IN CLINICAL VARIANTS OF FRONTOTEMPORAL LOBAR DEGENERATION

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Background and Aims:: We aimed to assess longitudinal patterns of atrophy shown by magnetic resonance imaging (MRI) in the cortical and subcortical GM of patients affected by different clinical variants of the FTLD spectrum.

Methods:: Fifty-nine patients, including 26 with behavioral variant of frontotemporal dementia (bvFTD), 10 non-fluent/agrammatic variant of primary progressive aphasia (nfvPPA), 12 semantic PPA (svPPA), and 11 motor neuron disease (MND), underwent MRI on a 3T scanner at 6-month intervals for one year. Thirty-three healthy controls underwent the same protocol. 3D T1-weighted MRI sequences were analyzed using voxel-based morphometry to assess the longitudinal evolution of GM atrophy in patients, compared with HC.

Results:: At baseline, severe diffuse atrophy of frontotemporal cortical regions and basal ganglia was found in bvFTD, nfvPPA and svPPA groups, whereas MND did not show significant GM atrophy. At 6-month follow-up, bvFTD and PPA showed progression of atrophy in the insular (bvFTD, nfvPPA and svPPA) and anterior cingulate cortices (bvFTD and nfvPPA), bilaterally, as well as in the left caudate nucleus and middle temporal cortex (svPPA). At 12-month follow-up, similar patterns of atrophy progression were found, with the additional involvement of the superior frontal cortical gyri in nfvPPA, and right hippocampus in svPPA. No significant progression of atrophy was found in MND.

Conclusions:: Atrophy of insular and anterior cingulate cortical regions closely reflects the progression of neurodegeneration across the behavioral and linguistic presentations of FTLD, in contrast with a substantial sparing of GM in MND. Funding: European Research Council (StG-2016_714388_NeuroTRACK).
IMPROVED ASSESSMENT OF LONGITUDINAL SPINAL CORD ATROPHY IN MULTIPLE SCLEROSIS USING A REGISTRATION-BASED APPROACH: RELEVANCE FOR CLINICAL STUDIES

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Background and Aims:: Reliable measurements of cervical cord atrophy progression may be useful for monitoring neurodegeneration in multiple sclerosis (MS). Here, we compared a new, registration-based (Reg) method with two existing methods (active surface [AS] and PropSeg) to measure cord atrophy changes over time in MS patients.

Methods:: Cervical cord 3D T1-weighted scans were collected at baseline and after 1.13 years median follow-up (range=0.7-3.2 years) from one cohort acquired at 1.5T (8 healthy controls [HC]/28 MS patients), and one cohort acquired at 3.0T at three European sites (25 HC/67 MS patients). The Reg method included an accurate registration of baseline and follow-up straightened cord images, followed by optimized cord segmentation using the AS method. Cross-sectional areas (CSA) from Reg, AS and PropSeg were used for sample size calculations. Intra- and inter-observer agreement of Reg and AS was also assessed.

Results:: Percentage CSA changes (PCSAC) and related standard deviations (SDs) were lower with Reg than with the other methods. For example, PCSAC in relapsing-remitting MS patients at 3.0T was -0.82% (SD=1.67) with Reg, -0.98% (SD=2.32) with AS and -1.24 (SD=3.93) with PropSeg. This was reflected in a lower sample size, being n=232 with Reg, n=354 with AS and n=885 with PropSeg in this population to detect a 50% treatment effect. Intra- and inter-observer agreement ranged from 0.72 to 0.91 with AS, while they were >0.99 with Reg method.

Conclusions:: Lower sample size and improved reproducibility support the use of the Registration method to measure cervical cord atrophy progression in future MS clinical studies.
MACRO- AND MICRO-STRUCTURAL CEREBELLAR AND CORTICAL CHARACTERISTICS OF COGNITIVE EMPATHY TOWARDS FICTIONAL CHARACTERS IN HEALTHY INDIVIDUALS

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Background and Aims:: Few investigations have analyzed the neuroanatomical substrates of empathic capacities in healthy subjects, and most of them have neglected the potential involvement of cerebellar areas. The main aim of the present study was to investigate the associations between bilateral cerebellar structural measures and levels of cognitive and affective trait empathy.

Methods:: We estimated macro- and micro-structural morphometric variations of cerebellar and cerebral Gray Matter structures in a sample of 70 healthy subjects of both sexes, tested by Interpersonal Reactivity Index (IRI) to ascertain whether the potential empathy-related peculiarities in cerebellar areas were accompanied by structural differences in other cerebral regions. At a macro-structural level, volumetric differences were analyzed by Voxel-Based Morphometry and Region of Interest-based approaches, and at a micro-structural level, we analyzed Diffusion Tensor Imaging (DTI) data, focusing on Mean Diffusivity (MD) and Fractional Anisotropy.

Results:: Fantasy IRI-subscale (which examines participants’ abilities to imaginatively transpose themselves into feelings and actions of fictitious characters) was found to be positively associated with volumes in right cerebellar Crus2 and pars triangularis of inferior frontal gyrus (figure1). DTI analyses revealed cerebellar Crus2 MD values negatively associated with Fantasy IRI subscale scores (figure2).
Conclusions:: Cerebellar engagement in Fantasy IRI subscale highlights its involvement in socio-cognitive processes and supports the view of a "social cerebellum", and specifically of an "empathic cerebellum". Then, morphological variations of cerebellar Crus2 and pars triangularis allow to extend the traditional cortico-centric view of cognitive empathy to the cerebellum and indicate that in empathizing with fictional characters the cerebellar and frontal areas are co-recruited.
VOLUMETRIC ANALYSIS OF HIPPOCAMPAL VOLUME: CORRELATION WITH BDNF - VAL66MET POLYMORPHISM AND COGNITIVE IMPAIRMENT IN SOUTH INDIAN PD PATIENTS

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Background and Aims:: Brain-derived neurotrophic factor (BDNF) is a neurotrophin that plays role in neurogenesis and synaptic plasticity of the hippocampus. To calculate the hippocampal volume, association with BDNF (Val66Met) polymorphism, and correlation with cognitive impairment.

Methods:: 90 PD patients were recruited and scanned for 3Tesla MRI. T2 images used to calculate the volume manually using the Syngovia workstation.

Results:: The average of right and left hippocampal volumes was 3.67±0.49 Cm$^3$ where, the right hippocampal volume (3.76 ± 0.48 Cm$^3$, p=0.02) was significantly higher than the left (3.58 ± 0.55 Cm$^3$). Hippocampal volume was compared among males and females where right hippocampal volume (3.83±0.46 Cm$^3$, p=0.05) of males was significantly high compared to females (3.56±0.55 Cm$^3$). The low hippocampal volume group found to have a significantly high UPDRS III ON score (16.78±5.25; p=0.0009) and significantly high cognitive impairment (25.91±3.08; p=0.01). Wild genotype G/G of BDNF Val66Met frequency was higher i.e., 56.7% followed by heterozygous G/A 31.1% and mutant A/A genotypes 12.2%. Mutant A/A genotype found to have (6.50±1.58 years; p=0.03) significantly lower disease duration and lower right (3.45±0.56 Cm$^3$, p=0.03), left (3.35±0.58 Cm$^3$, p=0.05) hippocampal volumes. The average hippocampal volume was positively correlated with the MoCA score (r=0.2193, p=0.03) indicating that reduction in volume reduces the MoCA score.

Conclusions:: Our study suggests the significant association of hippocampal volume with BDNF Val66Met polymorphism and cognitive impairment in south Indian PD patients.
ABNORMAL CORTICAL AND SUBCORTICAL STRUCTURE IN JUVENILE MYOCLONIC EPILEPSY DEMONSTRATED WITH ADVANCED MRI ANALYSIS

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Background and Aims:: Juvenile myoclonic epilepsy (JME) is the most frequent genetic generalized epilepsy syndrome. It typically occurs during adolescence with predominant myoclonic seizures, variably intermixed with generalized tonic-clonic and absences. Neurophysiological, neuropsychological and imaging studies in JME have shown focal abnormalities in the medial and dorsolateral prefrontal lobe. Our study’s aim was to explore for additional evidence of focal cortical abnormalities in JME using advanced neuroimaging techniques.

Methods:: We enrolled 16 consecutive patients (9 women, mean age: 30.2±10.4 years) with JME, and 16 age and sex-matched controls. All subjects underwent 3T MR study using standard protocol, including T1-3D Turbo Field Echo images with 1 mm thickness, to measure surface and thickness of several cortical Regions of Interest (ROIs) and volumes of several subcortical ROIs. Subcortical GM structures volumes were extracted and vertex-wise shape analysis was performed using standard Freesurfer analysis. 158 quantitative parameters were analysed.

Results:: Thirteen/158 variables presented significative differences between the two groups. In patients with JME, we observed bilateral volumetric reduction of thalami, putamina, nuclei caudati, nuclei accumbentes and bilateral increase in pallidal volume. Moreover, we found decreased right pars opercularis surface and left medial orbitrofrontal cortex thickness, along with increased left frontal pole surface.

Conclusions:: Our study found significative thalamic volumetric alterations in JME; dysregulation of fronto-thalamic network is considered a causative mechanism underlying seizures in this syndrome, due to the lack of inhibitory thalamic output towards cortical structures. We also found significative volumetric differences in basal ganglia, whose modulatory role on cortical excitability has recently been advocated.
WHITE MATTER LESION CHARACTERISTICS ON MRI CAN DIFFERENTIATE MULTIPLE SCLEROSIS FROM PATENT FORAMEN OVALE

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Background and Aims:: It is important to identify brain MRI features to help differentiating white matter lesions (WMLs) associated with demyelination and vascular mimics. We aimed here to find differences in MRI characteristics of WMLs occurring in multiple sclerosis (MS) and in patients with patent foramen ovale (PFO).

Methods:: 13 patients with MS (10 F, mean age: 47 years) and 13 with PFO with WMLs (10 F, mean age: 47) underwent 3T brain MRI, including FLAIR, 3D-T1, and SWI sequences. Each WML was first identified on FLAIR and classified considering topography, size (punctate, >3mm, or >10mm), shape (rounded or oval); subsequently, the presence of a correspondent hypointensity on T1 and the central vein sign (CVS) on SWI were assessed. Linear regression was used to compare lesion characteristics between diseases, stepwise logistic regression models to assess the association between lesion characteristics and disease type.

Results:: In MS, a total of 298 WMLs were detected, while in PFO 210 WMLs. The number of lesions located in the infratentorial and periventricular regions was higher in MS than PFO. They measured >10mm, had oval shape, were largely hypointense and showed the CVS. Instead, WMLs form PFO were mostly located in the deep white matter, were punctate and with a rounded shape in PFO. The combination of infratentorial location, oval shape, hypointensity and CVS best discriminated MS from PFO (accuracy 78%, specificity 87%, sensitivity 72%, p=0.02).

Conclusions:: The combination of different WML characteristics can facilitate an accurate differentiation between MS and PFO.
Background and Aims:: Posterior reversible encephalopathy syndrome (PRES) is an heterogeneous syndrome with the neurologic symptoms of hypertensive encephalopathy. In the majority of cases has typical MRI radiological landmark corresponding to edema that is classically parieto-occipital. Rare are the form with spinal cord involvement (PRES-SCI).

Methods:: A 27 year-old bengalis man arrived at the emergency department of our hospital because two weeks previous presents lumbar pain, lower limb weakness and paresthesia, mild urinary retention. These were followed by mild headache and visual loss. Neurological examination disclosed severe visual reduction and diffuse increase of tendon reflex. The past medical history was unremarkable. At the time of examination, his blood pressure was 240/130mmHg. The optic fundus examination disclosed signs of bilateral hypertensive retinopathy grade 3°. Serum electrolytes were normal except for severe hypokaliemia and mild hyponatriemia while kidney function tests were normal. MRI of the brain and spine revealed a hyperintense signal of medulla and spinal cord on T2 and FLAIR images The lesions were also hyperintense on diffusion-weighted imaging. As there was no clinical or lab evidence to support the diagnosis of encephalomyelitis or acute disseminating encephalomyelitis. Blood pressure was normalized, and the patient became asymptomatic few days. An MRI at 2 weeks revealed that the spinal cord changes were completely reversed.

Results:: A PRES-SCI was considered as the most plausible diagnostic possibility.

Conclusions:: PRES is a disorder of cerebral blood autoregulation and endothelial function causing vasogenic edema, occurring by an uncertain mechanism. Similar arterial regulatory mechanisms appear to occur in the spinal cord unusual finding.
Background and Aims:: Reporting age-related changes in neuroimaging findings is challenging. There is no clinical thresholds for normalized brain volumes. Assessing individual cases non-adjusted in size is even more difficult. We aimed to provide neuroradiologists a concise model of aging of the Central Nervous System (CNS) to simplify an assessment of structural features related to age.

Methods:: With CAT-12 and LST-2.0 we segmented 231 brain MRI scans of healthy participants (4–83 yo). To examine age-related changes of the CNS composition we built the ordinary least squares regression trendlines. To study the velocity of atrophic changes in brain compartments, we divided the study cohort into age groups: Adolescents < 20, Young adults (YA) ∈ [20, 40), Midlife adults (MA) ∈ [40, 60) and Older adults (OA) ≥ 60 yo. For brain structural estimates we built trendlines using non-linear Locally Weighted Scatterplot Smoothing and tested data for statistically significant differences between slopes. The volumes of cerebrospinal fluid (CSF), white (WM) and gray matter (GM) were expressed as fractions of intracranial volume. Intraventricular CSF (iCSF) was counted in proportion to cerebral CSF.

Results:: CSF% raised significantly (p<0.05) quicker in YO and OA compared to the general population. In OA there was a significant increase in iCSF%. Cortical and total GM% decreased across the life with a significantly faster pace in adolescents and OA. The dynamics for WM% were opposite with a significantly different slope for adolescents.

Conclusions:: Building a model of age-related brain atrophy will help distinguish the normal brain aging from the accelerated one.
Dynamic Cognitive Reserve in the Adult Lifespan

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Background and Aims:: The relationship between brain and cognition is dynamic and may change across the lifespan. Age-related changes in brain structure/function are tied to changes in cognitive efficiency in normal aging, although the factors contributing to inter-subject differences have been scarcely investigated. One of the heuristics explaining such variance in cognitive aging is reserve (Stern et al., 2020), a construct suggesting that dynamic cognitive and underlying structural/functional brain processes cope with age-related brain changes in determining cognitive functioning. Here we investigated, in a large (N=197) cross-sectional sample of healthy adults across the lifespan (18-77 years), the impact of age on dynamic cognitive reserve (dCR), i.e. measured cognitive abilities after confounding factors (gender, socio-economic status, brain volume and vascular lesion burden) have been removed.

Methods:: Neurocognitive/neuroimaging data were analyzed in univariate ANOVAs including age and gender, confounding factors, and their interactions, as to investigate the mediating effect of static cognitive and brain reserve on cognitive efficiency. Multivariate regression models also explored the differential impact of included variables on cognitive abilities.

Results:: We found a general effect of age on dCR, and specific interactions with other factors as for example, efficiency in set-switching was better predicted in females, by a model including age, static cognitive reserve and vascular lesion burden as predictors.

Conclusions:: Understanding the dynamics of age-related cognitive changes can lead to optimized detection and intervention methods of addressing cognitive decline. Moreover, the way has been paved for further investigating the role of brain micro/macrostructure in cognitive aging and decline processes.
A CASE OF ENCEPHALOPATHY WITH REVERSIBLE SPLENIAL LESION OF THE CORPUS CALLOSUM

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Background and Aims:: The concept of mild encephalopathy with reversible splenial lesion (MERS) was identified for the first time as a rare clinic-radiological syndrome by Tada et al in 2004. It is classified in MERS type I and MERS type II, depending on the involvement of the splenium of the corpus callosum (SCC) alone or also other white matter areas. The exact pathophysiology is unknown; however, infectious-related MERS remains the most common cause of reversible splenial lesions in childhood.

Methods:: A previously healthy 22-year-old women was admitted to our hospital due to a 2-days history of headaches and confusion associated with fever. Neurological examination revealed neck stiffness without localizing signs. Chemistry panel showed an elevated blood white cell counts. Brain MRI showed isolated abnormal signals in the SCC without contrast enhancing. The examination of cerebrospinal fluid revealed lymphocytic meningitis without common bacterial or viral agents. After combined antiviral and antibiotic treatments, the symptoms resolved within 7 days and the follow-up MRI, taken 28 days after the initial examination, demonstrated resolution of the lesion.

Results:: MERS is characterized by a transient mild encephalopathy and MRI findings of a reversible lesion in the SCC. The syndrome mainly affects children and young adults. Fever, confusion and headaches are the most common clinical manifestation like in our case. The major cause is infection by virus or bacteria.

Conclusions:: Psychiatrist and neurologist should be aware about the presence of confusion, isolated lesion in the SCC and lymphocytic meningitis suggesting the diagnosis of MERS.
T1-HYPERINTENSITY IN THE PULVINAR UNRELATED TO FABRY DISEASE OR OTHER CAUSES OF BASAL GANGLIA MINERALIZATION: A CASE REPORT

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Background and Aims:: Hyperintensity in both pulvinar nuclei in T1-weighted MRI sequence, known as “Pulvinar sign” (PS), is usually considered a pathognomonic sign of Fabry disease (FD). We describe a patient with PS unrelated to FD or other causes of basal ganglia mineralization.

Methods:: Case report. A 41-year-old man presented with left arm weakness and neck pain after an abrupt movement during gardening. The neurological examination was unremarkable. His medical history was significant for Klinefelter Syndrome, bradyarrhythmia, prior deep venous thrombosis of lower limbs, hypertension, and dyslipidemia. A 1.5 T brain magnetic resonance imaging (MRI) showed T1-hyperintensity in the posterior thalamus bilaterally, more pronounced in the pulvinar, with symmetrical and bilateral areas of T2* signal void in the globus pallidus (fig.1); it showed also multiple small areas of gliosis in the white matter. MRI findings and the history of bradyarrhythmia in this patient raised suspicion of possible FD. Specific hematological and genetic enzymatic activity tests were thus required.
Results: Calcium and parathyroid hormone, glucose, serum iron, ferritin, transferrin, and ammonia levels were within normal ranges, screening for vasculitis and autoimmune disorders was unremarkable, and human immunodeficiency virus was excluded on serology testing. There was a slight reduction of leukocyte a-galactosidase A with normal plasma lyso-Gb3 concentration. FD and other causes of basal ganglia mineralization were excluded.

Conclusions: The “pulvinar sign” can be unrelated to FD or other disorders leading to basal ganglia mineralization. This sign is not pathognomonic of specific conditions and should be interpreted in the context of the whole clinical picture.
CHANGES IN DEFAULT MODE NETWORK CONNECTIVITY IN PATIENTS WITH POSTMASTECTOMY SYNDROME

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Background and Aims:: In the modern concept of postmastectomy syndrome (PMES), more attention is paid to the neuropsychiatric component, which observed in more than 90% of patients. Resting state functional magnetic resonance imaging (rs-fMRI) is a promising technique for detecting initial changes of the functional connectivity of brain neural networks in these patients. The aim of the study was to assess changes in the functional connectivity of the default mode network in patients with PMES using resting state functional MRI (rs-fMRI).

Methods:: 25 women in the late postoperative period (>6 months) after radical mastectomy for breast cancer and 25 healthy women (control group) were underwent a clinical examination with an assessment of complaints, anamnesis and questionnaires for depression, anxiety, pain syndrome, quality of life and standard and rs-fMRI on 3.0T MR-scanner.

Results:: In patients with PMES, a functional reorganization of neural networks with the involvement of DMN with a predominance of processes of separation of intra- and interhemispheric connections was revealed (p<0.001). There was a decrease in functional connections between the medial prefrontal cortex (the key structure of the DMN) and a number of important centers of the brain (hippocampus, cerebellum, medial thalamic nuclei, subcallosal cortex, middle temporal gyrus cortex), which are responsible for the regulation of cognitive processes, emotions, memory.

Conclusions:: The data obtained indicate a functional reorganization of the resting state neural networks of the brain in PMES patients in comparison with healthy volunteers and require further study.
EXTENSIVE TRACTOPATHY WITH ANTERIOR CORD INVOLVEMENT AND “INVERTED V SIGN” IN B12 DEFICIENCY DUE TO PERNICIOUS ANEMIA

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Background and Aims:: Background
Subacute combined degeneration of the cord (SACD) due to vitamin B12 deficiency typically causes demyelination of the dorsal and lateral spinal cord sparing the anterior portion. We present a Sri Lankan lady who developed severe SACD due to B12 deficiency with pernicious anemia. Her radiology demonstrated involvement of all tracts of the spinal cord including the anterior with the inverted V sign.

Methods:: A 49 years old non vegetarian woman presented with marked upper and lower limb weakness and numbness for 2 years. She was pale and pigmented. She had flaccid paraparesis of the lower limbs. Distal motor weakness was noted in the upper limbs. All sensory modalities of the lower limbs were impaired.

Results::

Blood picture revealed severe macrocytic anemia with hyper-segmented neutrophils. Bone marrow examination demonstrated a megaloblastic marrow with giant metamyelocytes and erythroid hyperplasia. Serum vitamin B12 was low 67 (140 -650mol/l). MRI spine demonstrated significant high signal intensities in anterior, lateral and dorsal columns with white matter changes in brain. Dorsal column hyperintensity specifically showed the inverted V sign. Both intrinsic factor and parietal cell antibodies were positive. Severe SACD due to pernicious anemia was diagnosed. Treatment with vitamin B12 partially alleviated her symptoms.

Conclusions::
Tractopathy in vitamin B12 deficiency is rare. Involvement of the anterior column has been previously reported only in a single case study. Inverted V sign "rabbit ear sign" is a classic finding in SACD. Severe vitamin B12 deficiency if not detected early and treated could result in severe neurological sequel.

Figure 2
T2 Weighted MRI spine axial views (A,B) and sagittal view (C) showing hyperintensities in anterior, posterior and lateral columns suggestive of tractopathies. Hyper intense signals in dorsal column showing inverted "V" sign (D) seen in subacute combine degenerative of the cord. T2 Weighted MRI brain axial view (E) showing bilateral periventricular white matter hyperintensities in B12 deficiency.
LOCUS COERULEUS ASSESSMENT BY MRI: A COMPARISON OF THREE DIFFERENT APPROACHES

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Background and Aims:: This study aims to evaluate inter-individual differences in Locus Coeruleus (LC) MRI-contrast and volume through three different post-processing approaches.

Methods:: LC-MRI was acquired in 45 subjects (27M; 60-80 yrs) using a 2D Fast-Spin-Echo (FSE) T1-weighted sequence (TE/TR 14/600ms; flip-angle90°; voxel size 0.39x0.39x2.2mm; NEX5). Three different post-processing approaches for the LC analysis have been evaluated: a Semi-Automatic (SA), a Deep-Learning (DL) and a Template-Based (TB) one. Three different LC metrics were calculated using the SA, DL and TB methods: the normalized maximum intensity (LCmax), the mean intensity (LCmean) and the volume (LCvol) of the LC.

Results:: SA and DL methods analyzed the LC signal in the T1-w native space while the TB method offered the advantage of a high-resolution template (0.5 mm isotropic) and of loco-regional analysis. Pair-wise correlation between the three different post-processing approaches showed high degree of association in terms of LCmax and LCmean ("average r"=0.70) and moderate degree of association for LCvol ("average r"=0.44). The latter could be partly due to the different resolution of native and template spaces.

Conclusions:: Our results indicate a moderate-to-high degree of agreement between global LC analyses in native or template space, with the latter approach being seemingly more suitable for the LC loco-regional analysis.

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Background and Aims:: Vanishing brain space occupying lesion is defined as reduction or disappearance of a brain lesion spontaneously or after steroid treatment to ≤ 70% of its size before establishing its definitive diagnosis. Resolution of lesion leads to diagnostic and management challenge. Here we describe a case with a vanishing brain SOL which was radiologically suggestive of CNS lymphoma with inconclusive brain biopsy findings.

Methods:: 75-year-old woman presented with subacute onset right sided upper and lower limb weakness for two weeks. Examination detected, lower motor weakness on the affected side with normal sensory. Reflexes were diminished globally. Basic investigations were normal. NCS showed peripheral nerve demyelination. CSF analysis revealed lymphocytosis at 26 with elevated protein (64mg/dl). MRI brain detected homogeneous mass lesion in the posterior body of the corpus callosum which extended into parietal lobes on either side. This was hypo-intense on T1 and hyperintense on T2 & FLAIR images. Splenium of the corpus callosum was swollen. MRS showed Choline peak with reduced NAA levels. MRI was suggestive of a CNS lymphoma; however, CNS demyelination could not be ruled out in the presence of peripheral nerve demyelination. Therefore, she was given IV methyl prednisolone.

Results:: Brain biopsy findings after steroids were inconclusive. MRI at 4 weeks after steroids and subsequent imaging showed complete resolution of the lesion correlating with clinical improvement.

Conclusions:: Vanishing brain space occupying lesion is a rare radiological diagnosis which poses diagnostic and management challenge. Our patient highlights the importance of early histo-pathological diagnosis in CNS-SOL before steroid therapy.
Background and Aims:: Joubert syndrome (JS) is a rare autosomal recessive central nervous system malformation characterized by hypotonia, ataxia, abnormal psychomotor development and mental retardation, variable ophthalmologic features such as oculomotor apraxia and neonatal breathing abnormalities. Many patients die in infancy or childhood, but some survive into adulthood with variable cognitive and motor impairments. Radiographically it is characterized by “molar tooth sign” in MRI, includes cerebellar vermis hypoplasia or dysplasia, thick and horizontally oriented superior cerebellar peduncles, and abnormally deep interpeduncular fossa. A 34 year-old female presented in our institution with parental complaints of generalized chorea with difficulty in ambulation and speech. She had no problems in respiration or breathing. Neurological examination showed atrophic changes in both arms and feet, ptosis of the left eye, truncal ataxia, severe dysarthria, and global hyperreflexia. She was noted lack of appropriate awareness to surroundings and notably stuttering and severely dysarthric. Showing abnormal gait, major difficulty in walking that of the appearance of a staggering-like gait disorder.

Methods:: case report

Results:: Cranial MRI was done showing thickened and elongated superior cerebellar peduncle giving midbrain a molar tooth appearance; cerebellar vermis appeared mildly deformed. The diagnosis of Joubert syndrome was made based on patient’s history, physical examination, and pathognomonic neuroimaging features. No genetic testing done due to its unavailability in our institution.

Conclusions:: Joubert Syndrome is a rare autosomal recessive disease which affects approximately 1/80,000 to 1/100,000 people worldwide. This reported case is presented with hypotonia, abnormalities in gait and balance, developmental delay, and pathognomonic “molar tooth sign” in her MRI.
ACERULOPLASMINEMIA: A NOVEL SPLICING MUTATION PRESERVING THE GLOBUS PALLIDUS FROM IRON ACCUMULATION

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Background and Aims:: Hereditary aceruloplasminemia (HA) is a rare inherited disease caused by homozygous mutation of ceruloplasmin (CP) gene, characterized by brain iron overload. Hypointensity of MRI signal in thalami and basal ganglia, especially globus pallidus (GP) is considered a neuroimaging hallmark of this disease. Here, we report the case of two Italian cousins carrying a novel splicing homozygous mutation in intron 6 (IVS6+1 G>A) of CP gene

Methods:: Methods Genomic DNA was extracted from peripheral blood by standard methods. A written informed consent was obtained from each subjects involved in the study. The primers flanked all 19 exons and intron–exon boundaries of CP (NM_000096) were designed using the web site Primer 3 (http://bioinfo.ut.ee/primer3-0.4.0/). The purified PCR products were analyzed on 3500 Genetyc Analyzer (Life Technologies, Carlibad, CA, USA). The new identified mutation was checked in a control population of 200 ethnically matched controls. The MRI protocol included whole-brain, T1-weighted images DTI and conventional T2-weighted and FLAIR images.

Results::
Interestingly, the proband was symptomatic for neurological and visceral symptoms whereas his cousin was asymptomatic. MRI features in both patients were characterized by marked iron accumulation in the thalami and basal ganglia nuclei, while GP was spared. MRI performed in the proband at 2 and 4-years of follow-up, confirmed progressive neurodegeneration of thalami and basal ganglia without involvement of GP.

Conclusions: Our findings expand the phenotypic spectrum of this disease demonstrating that in HA-carriers of splicing homozygous mutation in intron 6, GP can remain spared by iron accumulation over time.
ACUTE CARBON MONOXIDE POISONING: MAGNETIC RESONANCE IMAGING FEATURES

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Background and Aims:: INTRODUCTION: Carbon monoxide (CO) intoxication is still one of the most frequent conditions causing brain damage as a result of hypoxia. Several neuropsychiatric features and cerebral magnetic resonance imaging (MRI) lesions were found in these patients. The aim of our study was to describe clinical and radiological features of CO intoxication.

Methods:: METHODOLOGY: A retrospective study of 4 years was performed, including patients who presented an acute CO intoxication. Clinical and cerebral MRI findings were collected and analysed.

Results:: RESULTS: Twenty-six patients were included (16 men and 10 women). The average age was 40 years old (11-82 years old). All patients presented mental status change with different severity. Repeated clinical examination revealed cortical visual impairment in four patients. Twelve patients had memory loss and five had extrapyramidal syndrome. Cerebral MRI had shown restricted diffusion of the bilateral globi pallidi in twelve patients (46%). Cerebral cortex, and fronto-parieto-occipital white matter were involved in five patients (19%). Four patients had bilateral lesions of hippocampi (15%). Two patients had an occlusion of the cerebral posterior artery and extracranial internal carotid with ischemic stroke lesions respectively. One patient had a lesion in the splenium of the corpus callosum. Nine patients had normal cerebral MRI (34%).

Conclusions:: CONCLUSION: Several clinical features may be caused by acute CO poisoning. Bilateral globi pallidi, cerebral cortical and cerebral white matter with restricted diffusion may be a characteristic MRI features in patients with CO intoxication.
LINKING STRUCTURAL AND FUNCTIONAL BRAIN ALTERATIONS IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS

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Background and Aims: Imaging studies have consistently but separately shown structural and functional brain alterations in patients with multiple sclerosis (MS), although an integrated understanding of them is currently lacking. We aim to provide a unified representation of the complex structural-functional scenario in the brain of patients with MS.

Methods: We included 100 patients with relapsing-remitting MS (median expanded disability status scale [EDSS]=1.5, cognitive impairment [CI] in 30%) and 43 normal controls. We applied an innovative data-driven “fusion” approach able to simultaneously modeling relationships and contributions across MRI modalities.

Results: Out of 20 linked structural-functional patterns across study population, only one (GM density: 41%; fractional anisotropy along WM tracts:42%; intra-network functional connectivity (FC) across brain: 17%) showed significant group difference, with a cross-modalities loading coefficient lower in MS than NC (-0.29±1.05 vs 0.69±0.34, corrected-p <0.004). This was already present at very early disease stage and particularly low in the MS subgroups with larger white matter (WM) lesion volume (>3.5 cm³), higher EDSS (>1.5), presence of CI and longer disease duration (>5 years). Overall, with worsening disease severity, relative contribution to the significant linked covarying pattern was decreasing for structural integrity and increasing for FC. Specific linked covarying patterns, mostly driven by altered intra-network FC, significantly explained EDSS and CI, especially attention and processing speed (adjusted R² = 0.62, p < 0.001).

Conclusions: These findings suggest the presence in the brain of MS patients with mild disability of multidimensional and clinically relevant “architectures” linking GM atrophy, WM tract damage and network functional reorganization.
ALTERED INTERPLAY AMONG LARGE-SCALE BRAIN FUNCTIONAL NETWORKS UNDERPINS MULTI-DOMAIN ANOSOGNOSIA IN EARLY-AD

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Background and Aims:: Decline in self-awareness (anosognosia) is a prevalent early symptom of Alzheimer’s disease (AD). The integrity of the functional hubs of the default mode network (DMN) has been heavily implicated in retained self-awareness abilities in AD patients. Moreover, an early breakdown of this network has been found to be a hallmark feature in the clinical profile of AD. However, the interplay among other large-scale brain networks in support of cognitive awareness in early-AD remains poorly understood.

Methods:: Resting-state functional MRI scans were acquired and pre-processed from fifty-three early-stage AD individuals. An independent component analysis isolated four intrinsic connectivity large-scale brain functional networks, namely left and right central executive fronto-parietal networks (FPN), salience network, anterior and posterior DMN. In addition, hypothesis-driven seed-based connectivity analyses were performed. Multiple regression models were carried out between scores of memory, non-memory (executive) and total anosognosia and large-scale network and seed-based connectivity maps.

Results:: All anosognosia domains displayed consistent lower fronto-temporal connectivity. However, higher connectivity was found between memory anosognosia and parieto-temporal regions. Non-memory anosognosia displayed stronger connectivity between the DMN-cerebellum and the contralateral prefrontal cortices. Finally, total anosognosia yielded increased connectivity between the right FPN and the anterior cingulate.

Conclusions:: Multi-domain anosognosia in early AD is characterised by selective fronto-temporal disconnection. Selectively increased fronto-parietal-subcortical connectivity seems to provide cognitive resources to cope with unawareness, explaining the heterogeneity of the symptom. Therefore, these findings support the hypothesis that alterations in functional connectivity of frontal regions involved in executive related mechanisms represent the neural correlate of domain-specific anosognosia in early AD.
DIFFERENT EYES, SAME BRAIN: A COMPARISON OF BRAIN VOLUMES BETWEEN CHINESE AND CAUCASIANS

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Background and Aims:: Differences in brain volume (BV) between Chinese and Caucasian populations remain largely unexplored. This might be due, at least in part, to the lack of robust normalization and harmonization of multi-site lifespan MRI data with varying acquisition protocols. We aim to assess here differences in site- and scanning harmonized MRI-derived brain volumes in a large lifespan population of Chinese and Caucasian healthy subjects (HS).

Methods:: A multi-center 3T Siemens MRI dataset of 1829 Chinese HS (aged 15-80 years old, 55.9% women) and 3234 Caucasian HS (aged 15-88 years old, 52.4% women) was collected from 2 research groups worldwide and from 19 open-source datasets. Normalized (for head size) volumes of the whole brain (NBV), grey matter (NGMV), white matter (NWMV), lobes and thalamus were assessed using SIENAX2.0. Lifespan trajectories of site and scanning variances harmonized volumes were derived with multivariate regression, including age (with quadratic and cubic terms), gender, ethnicity and interactions as predictors.

Results:: Chinese and Caucasian did not differ in any structure except for higher temporal lobe volume in Chinese (β=0.784, 95% confidence interval [CI]: 0.319-1.248, p<0.001). In all subjects, with increasing age, both NBV ($R^2=0.54$, p<0.001) and thalamus ($R^2=0.30$, p<0.001) decrease linearly, while NGMV ($R^2=0.66$, p<0.001) and NWMV ($R^2=0.12$, p<0.001) decrease quadratically.
Conclusions: Age-related volume trajectories of Chinese and Caucasian brains are very similar. The difference in temporal lobe volume between the two populations needs further analysis to ascertain whether or not they may reflect ethnicity-related influence on brain structures.
MICRO-STRUCTURAL ALTERATION OF SUBSTANTIA NIGRA IN PARKINSON'S DISEASE; A 7 TESLA MRI STUDY

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Background and Aims:: Dopamine-containing neurons in Parkinson's disease (PD) degenerate in different parts of substantia nigra (SN) to different degrees. The maximal neuron loss occurs in nigrosome-1, which is considered as a diagnostic biomarker in PD with iron-sensitive MRI techniques. However, clinical correlates of iron accumulation in nigrosome-1 remain unknown. Here, we measured quantitative susceptibility mapping (QSM) of nigrosome-1 using a 7 Tesla MRI and computed correlation with motor symptoms and with striatal dopamine terminal degeneration using 123I-ioflupane SPECT, to identify the clinical parameter that reflects nigrosome-1 degeneration.

Methods:: 57 PD patients and age-, sex-matched 56 healthy control subjects (HC) were recruited. Three-dimensional QSM and T1 weighted images were acquired using a 7 tesla MRI scanner. 54 PD patients also underwent 123I-ioflupane SPECT. QSM images were registered to standard space and permutation analysis was performed to elucidate the alteration within the SN in PD compared to HC.

Results:: PD patients showed higher QSM values within the dorsolateral part of SN compared to HC, which correspond to nigrosome-1. MDS-UPDRS part 3 score showed a positive correlation with the QSM value of nigrosome-1 (p < 0.05). Furthermore, the striatal uptake ratio of 123I-ioflupane SPECT showed a significant negative correlation with the QSM value of nigrosome-1 (p < 0.005).

Conclusions:: The present findings suggest that alteration of nigrosome-1 detected by QSM corresponds to the motor disabilities and the severity of terminal degeneration of dopaminergic neurons in the striatum of PD.
ACCURACY OF BEDSIDE SONOGRAPHIC MEASUREMENT OF OPTIC NERVE SHEATH DIAMETER FOR INTRACRANIAL HYPERTENSION DIAGNOSIS IN THE EMERGENCY DEPARTMENT

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Background and Aims:: Ultrasound measurement of optic nerve sheath diameter (US ONSD) has been proposed as a method to estimate elevated intracranial pressure (ICP) even if the optimal ONSD threshold is nowadays unclear. The aim of this study is to assess the accuracy of ONSD, as compared to head computed tomography (CT), in detecting elevated ICP on both Traumatic and Non-Traumatic Brain Injury (TBI).

Methods:: This is an ongoing, prospective, cross-sectional, multicenter study. Patients presenting to emergency department (ED) for an Acute Brain Injury underwent to ultrasound ONSD measurement and urgent CT scan. Sensitivity and specificity of US ONSD is calculated using CT as reference standard considering 5.5 mm OSND threshold.

Results:: To date 64 patients were enrolled. CT was ABNORMAL in 14.1% of cases and ONSD was positive in all of these, achieving a sensitivity of 100% and a negative predictive value of 100%. Instead CT was negative in 85.9% of cases while ONSD measurement was positive in 78.2% of these, achieving a specificity of 29% and a positive predictive value of 17%.

Table 1: Sn = sensitivity, Sp = specificity, PPV = positive predictive value, NPV = negative predictive value, LR = likelihood ratio.

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>Sn (95% CI)</th>
<th>Sp (95% CI)</th>
<th>VPP (95% CI)</th>
<th>VPN (95% CI)</th>
<th>LR +</th>
<th>LR -</th>
</tr>
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<tbody>
<tr>
<td>≥ 5.5</td>
<td>100% (100; 100)</td>
<td>22% (12; 32)</td>
<td>17% (8; 27)</td>
<td>100% (100; 100)</td>
<td>1.3</td>
<td>0</td>
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</table>

Conclusions:: Our data suggest good sensitivity and a good negative predictive value of ONSD. In limited-resources contexts a negative US ONSD could allow emergency physicians to rule out elevated ICP in low risk patients, deferring CT. Furthermore in out-of-hospital setting a negative US ONSD could help clinicians to exclude an immediate neurosurgical need for Traumatic Brain Injury patients avoiding unnecessary centralization in Hub hospitals.
ROLE OF NEUROSPECIFIC PROTEINS IN THE PATHOGENESIS OF PARKINSONISM SYNDROME DEVELOPMENT IN CHRONIC BRAIN ISCHEMIA

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Background and Aims:: Background: Autoimmune reactions are important pathogenic part for parkinsonism syndrome in chronic brain ischemia (CBI). Aims: To reveal significance of the measurement of levels of autoantibodies to neurospecific protein S100 and myelin basic protein (MBP) in blood serum of patients with parkinsonism syndrome in CBI.

Methods:: Material and methods of research: In 52 (72.2%) patients with CBI associated with parkinsonism syndrome we analyzed autoantibodies to neurospecific protein S100 and MBP. Biochemical findings were compared with data of control group, consisted of 20 (27.8%) practically healthy donors.

Results:: Results and discussion: The investigations showed that the levels of autoantibodies to S100 were 119.85±3.38 IU (P<0.05), and to MBP 124.42±3.00 IU (P<0.001) that is higher than control values, accounted 68.22±3.53 IU and 55.69±4.74 IU, respectively.

Conclusions:: Conclusion: Biochemical investigations revealed increase in the level of autoantibodies to protein S100 and MBP in patients with parkinsonism syndrome in CBI. This is evidence of the role of neurospecific proteins in the pathogenesis of development of vascular parkinsonism. The study of protein S100 is useful both for monitoring and determination of the prognosis for disease development. These biochemical indicators may be used with diagnostic and prognostic purpose in chronic disorders of cerebral circulation, as well as optimization of therapeutic tactics for such patients.
PROGRESSION TO MIXED CEREBRAL MICROBLEEDS IN PATIENTS WITH COGNITIVE IMPAIRMENT WITH MULTIPLE STRICTLY LOBAR MICROBLEEDS

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Background and Aims:: Cerebral microbleed (CMB) is one of the neuroimaging markers of cerebral small vessel disease (SVD). Multiple strictly lobar CMBs are thought to be caused by cerebral amyloid angiopathy (CAA). Mixed CMBs are thought to be due to hypertensive arteriopathy (HA), but it has also been pointed out that CAA may coexist. Here we examined changes in CMBs distribution over time in patients with cognitive impairment with multiple strictly lobar microbleeds.

Methods:: We retrospectively evaluated MRI findings in 19 patients (mean age 80.9 years) with cognitive impairment with multiple strictly lobar microbleeds, which had been taken multiple MRIs scans at intervals of 1-5 years. The CAA-SVD score, which reflects the severity of CAA, was calculated according to a previously reported scoring system (Charidimou A, JAMA Neurol 2016).

Results:: Thirteen of 19 patients (68.4%) had an increased number of CMBs, and 10 of them (76.9%) had hypertension. The median CAA-SVD score at the first MRI scan was 3.0 in patients with increased CMBs. In 4 of 13 patients (30.8%) with increased CMBs, new CMB appeared in the deep region resulting in mixed CMBs. Cortical superficial siderosis newly emerged in one of these four patients.

Conclusions:: In the four patients which progressed to mixed CMB imaging findings, coexistence of HA and CAA, or alternatively, progression of CAA itself was suspected. Even in patients with CAA in the background pathology, imaging findings of mixed CMBs may be presented depending on the timing of MRI scan.
CONFIRMATION OF THE NEUROIMAGING SIGNIFICANCE OF ASYMPTOMATIC TRANSIENT ISCHEMIC ATTACK (TIA) IN THE COURSE AND PROGNOSIS OF ISCHEMIC STROKE

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Background and Aims:: To study the role of asymptomatic areas on MRI in the course of future strokes and their prognosis in patients with multiple anamnesis of TIA.

Methods:: MRI and MSCT-angiography were performed in 64 patients aged 50-70 years (average age-59.78±0.77) who had 3 or more TIAs in their anamnesis. Group 1 included 31 (48.4%) patients with only arterial hypertension and cerebral atherosclerosis, and group 2 included 33 (51.6%) patients with arterial hypertension, cerebral atherosclerosis, diabetes and coronary heart disease.

Results:: In group 1: bilateral lacunar ischemia were detected in 9 (29.1%) patients, in 8 (25.8%) and 14 (45.1%) were in the unilateral carotid and vertebrobasilar pool, respectively. In group 2, the lacunar ischemia were detected in 20 (60.6%) patients, in 8 (24.2%) in the carotid pool, and in 6 (18.2%) in the vertebrobasilar pool. In all groups of patients, stenosis and vascular deformity on MSCT-angiography did not correlate with the localization of cerebral changes on MRI. Among observed patients, 38.7% (in group 1) and 63.6% (in group 2) had cerebrovascular accident with severe neurological deficit within 2 years, which directly correlated with the speed of recovery and the size of asymptomatic ischemic areas.

Conclusions:: MRI and Multispiral CT-angiography should be performed regardless of the presence of changes in neurological status and any cerebrovascular problems. The identified changes later play an important role in the regression and prognosis of the disease, the solution of rehabilitation problems, when there is a significant stroke clinic with a large neurological deficit.
CEREBRAL SMALL VESSEL DISEASE IS DETECTABLE ON 3.0 TESLA MAGNETIC RESONANCE IMAGING: ESTABLISHED 3.0 TESLA MAGNETIC RESONANCE IMAGING FIRST TIME IN MONGOLIA

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Background and Aims:: Cerebral small vessel disease (CSVD) is a common neurological disease in older people. For patients diagnosed with small vessel disease by CT brain, for the first time in Mongolia, MRI brain (3.0 TESLA) was performed. The purpose of the study was to collect data from 58 patients aged 50-85 years old.

Methods:: In this descriptive study, we identified 56 elderly, aged between 50-85 years patients Small vessel disease was assessed on baseline computer tomography rating for leukoaraiosis and lacunes from our clinical data file from January 2021 to March 2021 at the Second general hospital of Mongolia. We assessed clinical features, sex, age, risk factors, and radiologic findings of these patients.

Results:: There were 56 patients with available brain MRI with 35 men and 23 women; mean age, 60.91±6.57 years. Features of the main clinical syndromes and MRI signs in patients with CSVD. The MRI measuring were including brain inflammation (2/3,4%) small subcortical infarcts (12 / 20.6 % ) lacunes microbleeds (7 cases/ 12%) enlarged perivascular spaces (6 cases/ 10,3% ), brain atrophy (12 cases/20,6% ) White Matter Hyperintensities (11cases/18,9% ) and Lacunar Infarct ( 8 cases/13,7% ).

Conclusions:: The study has the potential to further unravel the causes and consequences of changes in white matter integrity in elderly with CSVD by using new imaging techniques, MRI segmentation method capable of identifying multiple types of imaging features of CSVD and brain atrophy, we showed that WMH and lacunar had the greatest independent predictive value for vascular risk factors outcome in older individuals.
HYDRANENCEPHALY: A CASE REPORT OF A 32-YEAR-OLD WOMAN WITH PRESERVED WALKING ABILITY

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Background and Aims:: Hydranencephaly is a rare post-neurulation disorder characterized by the extensive hemispheric destruction with preservation of diencephalic and posterior cranial fossa structures. Brain matter is mostly replaced with a membranous sac filled with cerebrospinal fluid.

Methods:: A 32-year-old woman came to our attention for general assessment. She had a previous diagnosis of microencephaly of unknown origin. She was born at term. Her mother referred a severe psychomotor delay: she walked at 36 months after intensive fisiokinesitherapy and has never developed sphincter control and any form of speech. At neurological evaluation, she was able to walk with assistance, showing spastic gait. She was regularly fed by her mother. She opened her eyes spontaneously and turned her face in response to sounds. No meaningful actions were observed. She emitted only incomprehensible vocalization.

Results:: Comparative Genomic Hybridization did not reveal any chromosomal abnormalities. Electroencephalogram showed low amplitude and slowed activity. Brain MRI documented a severe telencephalic hypoplasia and cortical malformation with relative sparing of diencephalon and posterior fossa structures, consistent with the diagnosis of hydranencephaly. She died three months later, at the age of 32 years and 8 months, because of Sars-Cov19 pneumonia.

Conclusions:: Life expectancy in patients with hydranencephaly is very reduced. Most patients do not survive beyond the neonatal stage, nevertheless, some have been rarely diagnosed into adulthood. In these surviving cases, preserved brainstem regions maintain vital functions. Here we reported the case of one of the most long-lived patients affected by hydrancephalia with a surprising walking ability.
SPINAL EXTRADURAL ARACHNOID CYST: AN UNCOMMON CAUSE OF THORACIC SPINE COMPRESSION

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Background and Aims: Spinal extradural arachnoid cysts are unusual causes of symptomatic spinal cord compression. They represent expanding diverticula of the subarachnoid space herniating through a dural defect into the extradural space. The pathogenesis of this entity is still unclear.

Methods: We describe the clinical, neuroradiological and surgical aspects of two young patients in whom symptoms attributable to thoracic spine compression were caused by Spinal extradural arachnoid cysts.

Results: The first child presented with progressive spastic paraparesis accompanied by urinary incontinence, superficial and deep sensory disturbance below the umbilical level. The second patient presented with unstable gait as a result of weakness and diminished sensation in the lower extremities. Magnetic resonance imaging (MRI) showed a thoracic posterior extradural arachnoid cyst in both patients. The cyst was completely removed by posterior approach. Histological examination confirmed the diagnosis of arachnoid cyst. Neurological symptoms progressively resolved after surgical decompression.

Conclusions: Although quite rare, the diagnosis of arachnoid cyst should be included in the differential diagnosis of intraspinal extradural cystic lesions, causing spinal cord compression. Surgery is the treatment of choice, providing good clinical outcome.
HYPERTROPHIC PACHYMENINGITIS: A SINGLE ENTITY FOR A VARIETY OF NEURORADIOLOGICAL FINDINGS

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Background and Aims:: Hypertrophic pachymeningitis (HPM) is an infrequent disorder characterized by thickening of the dura mater with underlying processes of inflammation and fibrosis. The most frequent clinical manifestation is chronic headache, but it can also present several other neurological deficits.

Methods:: We present a case of HPM which presented as a deficit of the XII cranial nerve.

Results:: A 51-year-old man, previously diagnosed with catarrhal otitis media, came to our attention for the appearance in February 2019 of cervical/nuchal headaches, dysphagia, dysarthria and right deviation of the tongue: a contrast-enhanced brain MRI demonstrated a left infratentorial pachymeningitis, extended towards the foramen and the canal of the XII cranial nerve, and revealed a thrombosis of transverse and sigmoid sinuses. In July 2019 he underwent a subtotal petrosectomy, but the symptoms persisted and the postoperative contrast-enhanced brain MRI attested a worsening of the pachymeningitis with supratentorial involvement. He started a long-term treatment with oral steroids, achieving amelioration of the clinical manifestations; in October 2019 another MRI confirmed the clinical findings, showing a reduction of the supratentorial and infratentorial pachymeningeal thickening. While the microbiological screening was negative, positivity for serum IgG4 subclass was found. Upon suspicion of IgG4-related HPM a biopsy was performed (results in progress).

Conclusions:: We assessed how HPM can be accompanied by several and sometimes unusual neuroradiological findings, which can overlap in a single patient. Moreover, etiological assessing can be difficult: in our patient we hypotesized first an infectious disease, then a post-operative hypotension and finally a primary autoimmune etiology.
CORPUS CALLOSUM AGENESIS: ROLE OF FETAL MRI: A CASE REPORT AND REVIEW OF THE LITERATURE.

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Background and Aims:: INTRODUCTION: Corpus callosum agenesis is an important condition in man that can reveal numerous genetic syndromes. CASE REPORT: We report a case of diagnosis of isolated fetal corpus callosum agenesis (CCA). MRI improve prognosis evaluation, In our case MRI was confirmed isolated fetal corpus callosum agenesis. CONCLUSION: MRI appears to be an essential and reliable complement to fetal ultrasound in the event of suspected complete or partial agenesis of the corpus callosum and to search for associated malformations.

Methods:: Case report and review of literature

Results:: Prenatal MRI is a valuable complementary technique for either diagnosis of corpus callosum agenesis and depiction of associated neurologic abnormalities. In light of results and data reported in the literature, MRI appears to be an essential and reliable complement to fetal ultrasound in the event of suspected complete or partial agenesis of the corpus callosum and to search for associated malformations. Antenatal counselling in the event of diagnosis of agenesis of the corpus callosum is difficult because the individual prognosis remains poor.

Conclusions:: Prenatal MRI is a valuable complementary technique for either diagnosis of corpus callosum agenesis and depiction of associated neurologic abnormalities. In light of results and data reported in the literature, MRI appears to be an essential and reliable complement to fetal ultrasound in the event of suspected complete or partial agenesis of the corpus callosum and to search for associated malformations. Antenatal counselling in the event of diagnosis of agenesis of the corpus callosum is difficult because the individual prognosis remains poor.
DELPHI IN THE DETECTION OF NEUROLOGICAL CONDITIONS AND WHITE MATTER PATHOLOGIES

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**Background and Aims::** Evaluation of brain white matter fibers connectivity damage in stroke and traumatic brain injury (TBI) subjects by direct electrophysiological imaging (DELPHI) which analyzes TMS (transcranial magnetic stimulation) evoked potentials.

**Methods::** Study included 123 participants out of which: 53 subjects with white matter related pathologies of (39 stroke, 14 TBI) and 70 healthy age-related controls. All subjects underwent DELPHI brain network evaluations of TMS-EEG evoked potentials, and DTI scans for quantification of white matter microstructure fractional anisotropy.

**Results::** DELPHI output measures show a significant difference between healthy and stroke\|TBI groups, a multidimensional approach was able to classify healthy from unhealthy with a balanced accuracy of 0.81±0.02 and AUC of 0.88±0.01. Moreover, a multivariant regression model of DELPHI output measures achieved prediction of white matter microstructure changes measured by fractional anisotropy (FA) with highest correlations observed for fibers proximal to stimulation area such as frontal corpus callosum (r=0.7±0.02), anterior internal capsule (r=0.7±0.02) and fronto-occipital fasciculus (r=0.65±0.03).

**Conclusions::** These results indicate that features of TMS evoked response are correlated to white matter microstructure changes observed in pathological conditions such as stroke and TBI, and that a multi-dimensional approach combining these features in supervised learning methods serve as a strong indicator for abnormalities and changes in white matter integrity.
Background and Aims:: CT brain imaging is customary in clinical practice after Transient Ischemic Attack (TIA). However, NICE (2020) guidelines recommend MRI brain with diffusion weighted and blood-sensitive sequences; to be completed on the same day as the assessment. The aim of this audit was to assess the diagnostic radiology investigations performed on patients presenting with TIA to a university teaching hospital.

Methods:: We conducted a retrospective audit of all patients coded as TIA on the Hospital Inpatient-Enquiry (HIPE) system between July 2019 to July 2020. Data on brain imaging was accessed using the National Integrated Medical Imaging System (NIMIS) system. Hospital attendance records were accessed via the Emergency Department patient database. Data was analysed using Microsoft Excel.

Results:: One hundred and six patients had brain imaging performed (n=50 CT brain only; n=56 MRI only; n=49 CT and MRI). Of these patients, only eight had an MRI brain completed within twenty-four hours where Forty-eight patients had an MRI scans outside of twenty-four hours. Forty-nine patients had both a CT and MRI brain imaging performed. The median time to MRI brain was 2 days and 6 hours and the median time to CT brain was 2 hours and 45 minutes.

Conclusions:: This audit confirms duplication of TIA brain imaging and CT as the primary imaging tool for TIA which is not in keeping with best practice (NICE, 2020). This has implications for resources, radiation exposure and patient's length of stay. Development of dedicated ambulatory care pathways for TIA must incorporate rapid MRI access as the primary imaging modality.
CEREBROVASCULAR AUTOREGULATION IMPAIRMENTS DURING CARDIAC SURGERY WITH CARDIOPULMONARY BYPASS ARE ASSOCIATED WITH POSTOPERATIVE COGNITIVE DETERIORATION

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Background and Aims:: Post-operative cognitive dysfunction (POCD) occurs in 33–83% of patients after cardiac surgery with cardiopulmonary bypass (CPB). Intraoperative non-invasive monitoring of cerebrovascular autoregulation (CA) of individual patient may help to prevent POCD by detecting and control of optimal mean arterial blood pressure (optABP) or optimal cerebral perfusion pressure (optCPP). Objectives of the study are to investigate the association between CA dynamics and POCD.

Methods:: The study of non-invasive ultrasonic CA monitoring included 59 patients undergoing elective coronary artery bypass graft surgery with CPB. Non-invasive ultrasonic CA monitor for identification of real-time volumetric reactivity index (VRx(t)) was used in order to identify dynamics of CA changes. Feedback from CA monitor to surgical theatre will be used at first time in order to optimize dynamic control of optCPP(t) in our new prospective study.

Results:: 22 patients experienced POCD, 37 patients (63%) showed no cognitive deterioration. The duration of the single longest CA impairment (LCAI) event was associated with occurrence of POCD. The critical duration of the single longest CA impairment event was 5.02 min (odds ratio 14.5; CI 3.9-51.8). ROC area under curve 0.81, sensitivity 76%, specificity 82% has been shown for the duration of the LCAI event. Protocol of novel study with feedback will be presented.

Conclusions:: Prospective observational clinical study showed that too long patient-specific single CA impairment is associated with POCD. Novel prospective clinical study already started in order to get evidences that dynamic control of optABP keeping intact CA can decrease a rate of POCD.
CEREBRAL VENOUS THROMBOSIS IN BEHCET'S DISEASE. ABOUT 24 CASES

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**Background and Aims:** La thrombose veineuse cérébrale (TVC) est la manifestation la plus courante de l’angiobehçet qui peut être superficielle et / ou profonde. Le but de notre étude était d’évaluer les aspects épidémiologiques, cliniques, paracliniques, thérapeutiques et évolutifs de la CVT survenant dans la maladie de Behçet.

**Methods:** We report a retrospective study of 24 cases of CVT secondary to Behçet's disease, collected between 1999 and 2019 in the neurology department of military hospital Mohamed V (Rabat) Mohamed VI hospital (Marrakech). The diagnosis of Behçet disease was retained in all cases according to criteria established by the International Study Group for Behçet’s disease (1990). All the patients have benefit of symptomatic management, associated with antithrombotic and etiological treatment.

**Results:** La CVT représente 19,2% de toutes les manifestations neurologiques de la maladie de Behçet. Notre série est individualisée par la prédominance des localisations profondes dans 18 cas. Les manifestations cliniques étaient polymorphes, dominées par le déficit moteur pour les localisations profondes et l'hypertension intracrânienne pour les localisations superficielles. Les signes et symptômes moteurs étaient les résultats les plus courants au cours de l'évolution de la maladie, en accord avec les rapports précédents.

**Conclusions:** Grâce aux progrès de l'imagerie, en particulier de l'angiographie et de l'angio-IRM, le diagnostic de CVT est devenu incontournable. Une thérapie associant anticoagulation et prise en charge de la maladie de Behçet à base de corticostéroïdes et d'immunosuppresseurs a amélioré le pronostic de cette maladie mais avec une persistance de séquelles dominée par le déficit moteur partiel et la céphalée résiduelle.
THE CONTRIBUTION OF MRI IN BRAIN RADIONECROSIS AND POSTRADIQUE MYELOPATHY: ABOUT 15 CASES

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Background and Aims:: The brain and focal spinal cord radionecrosis are relatively rare but severe iatrogenic complications in patients irradiated for nasopharyngeal cancer. We proceed in this work to the description of the MRI brain radionecrosis and postradique myelopathy.

Methods:: The brain and focal spinal cord radionecrosis are relatively rare but severe iatrogenic complications in patients irradiated for nasopharyngeal cancer. We proceed in this work to the description of the MRI brain radionecrosis and postradique myelopathy.

Results:: Neurological complications are to type in 2 cases of myelitis, cerebellar necrosis in 3 cases, necrosis of the brain stem in 9 cases and temporal necrosis in 4 cases. The evolution is favorable after corticosteroid therapy in 6 patients and stationary in 9 patients.

Conclusions:: Imaging has a major role in the diagnosis of neurological complications of radiotherapy. However, MRI remains nonspecific and is the dynamic study of parenchymal brain perfusion which will allow one to distinguish between radionecrosis and tumor recurrence.
Background and Aims:: To identify and validate gray matter volume network in Alzheimer's disease (AD).

Methods:: We used two datasets. Training data were obtained with a 3-Tesla magnetic resonance machine (Trillium Oval, Hitachi) at Tokushima University and comprised 9 AD patients (women, 4; dementia, 7; mild cognitive impairment, 2; age, 66.7 ± 8.8 [mean ± SD] years) with positive amyloid positron emission tomography and 8 age-matched healthy controls (HCs). Validation data were obtained with a 1.5-Tesla machine (Vision, Siemens) in The Open Access Series of Imaging Studies and comprised 12 AD patients (women, 4; dementia, 12; age, 70.0 ± 3.7 years) and 12 age-matched HCs. We applied a principal component analysis-based algorithm, Scaled Subprofile Model, to gray matter volume data produced by voxel-based morphometry.

Results:: We identified a significant pattern from the training data, for which subject expression differed for the two groups (p=0.006; permutation test). It differentiated between the groups with 100% sensitivity and 100% specificity in the training (area under the curve =0.83, p =0.02) and with 83% sensitivity and 91% specificity in the validation (area under the curve =0.85, p =0.003). This network was represented by the principal components 1, 2, and 3 and showed relative decrease in the bilateral hippocampus, inferior temporal gyrus, inferior parietal lobes.

Conclusions:: We identified a AD-related gray matter volume network that captured relevant cortical regions, and validated it using data of a different machine and ethnic group, suggesting generalizability of the findings.
ANTI-GLUTAMATERGIC PROPERTY OF N-ACETYLCYSTEINE (NAC) DOCUMENTED IN VIVO IN THE HUMAN BRAIN USING PROTON MAGNETIC RESONANCE SPECTROSCOPY

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Background and Aims:: N-acetylcysteine (NAC), a cysteine prodrug and glutathione (GSH) synthesis precursor, is believed to have anti-glutamatergic properties for which direct in vivo evidence is lacking. To search for such evidence, the effect of 4 weeks of NAC supplementation on glutamate (Glu) and GSH levels was assessed in this study in vivo in the human brain using $^1$H magnetic resonance spectroscopy (MRS).

Methods:: Study participants consisted of 12 patients with chronic fatigue syndrome (CFS) and 12 healthy volunteer (HV) subjects. Each participant underwent baseline MRS scans (Fig. 1), and then was treated with 1800mg NAC/day for 4 weeks. After 4 weeks, $^1$H MRS scans were repeated to determine the effect of NAC supplementation on cortical Glu and GSH levels.

Results:: See Figure 2: At baseline GSH was 17% lower in CFS than HV (p=.04). Following 4 weeks of NAC treatment, GSH rose and normalized in CFS (p=.42), but was unchanged in HV (p=.33). Glu did not differ between groups at baseline (p=.24), but decreased in both CFS (p=.02) and HV (p=.04) after 4 weeks of NAC.

Figure 1
Conclusions:: Four weeks of NAC led to elevation of GSH levels in CFS only, while decreasing Glu levels in both CFS and HC, in support of NAC as an anti-glutamatergic agent. The concerted elevation of GSH and decrease of Glu suggest (Fig. 3) that NAC modulates Glu levels by deacetylating to Cys, whose bioavailability thus increases. Cys then combines with Glu to initiate GSH synthesis. Consistent with this study, the net effect is a decrease of total Glu.

Figure 2

Conclusions:: Four weeks of NAC led to elevation of GSH levels in CFS only, while decreasing Glu levels in both CFS and HC, in support of NAC as an anti-glutamatergic agent. The concerted elevation of GSH and decrease of Glu suggest (Fig. 3) that NAC modulates Glu levels by deacetylating to Cys, whose bioavailability thus increases. Cys then combines with Glu to initiate GSH synthesis. Consistent with this study, the net effect is a decrease of total Glu.
levels.

Figure 3
Background and Aims:: Automated brain volume analysis from MRI images, is gaining an important role in computer-aided diagnosis. This study compares the volumes of brain segments that measured by two automated brain analysis software: NeuroQuant and volBrain. The aim is to investigate the quantitative and qualitative reliability of automated brain analysis.

Methods:: We compared same brain segment volume measurements, from 45 patients, that calculated with both NeuroQuant and volBrain software. The statistical two-tailed unpaired t-test method used to determine if there is a significant difference on the same segment measurements performed from each software. Additionally, least square method used, to provide any evidence of linear correlation between them. In a case of extreme difference, manual volume measurement of a segment was performed, with JIM8 software.

Results:: From the comparison of brain segments volumetric measurements made by NeuroQuant and volBrain, the differences for the Intracranial Cavity considered extremely significant ($P=0.0001$), the Whole Brain considered not significant ($P=0.4690$), Cerebellum considered not significant ($P=0.2730$), White Matter considered quite significant ($P=0.0334$), Amygdala considered extremely significant ($P=0.0001$), Hippocampus considered not significant ($P=0.2332$), Putamen considered extremely significant ($P=0.0001$), Thalamus considered extremely significant ($P=0.0001$). In most cases strong linear correlation between the two software measurements found.

Conclusions:: The unexpected significant differences found in some segments raised questions about the reliability of automated volume analysis as a quantitative tool. Strong linear correlation of the volumes presents that both software finally provide good qualitative information on brain structures, which is an important factor for computed aided diagnosis.
Background and Aims:: We report a case of a young female with recurrent stroke-like episodes who developed disabling cerebral infarction which, after extensive aetiological investigation, was found to be caused by internal carotid artery (ICA) vasospasm. This rare condition is difficult to diagnose but has treatment implications and should be considered in the differential for idiopathic carotid territory stroke in young patients.

Methods:: A single case report.

Results:: A 32 year-old woman presented following a 5 year history of recurrent episodic hemiparesis affecting either side, and recurrent unilateral carotid watershed territory infarctions affecting both hemispheres. On this occasion she had presented with fluctuating consciousness, limb jerking and left hemiparesis. CT carotid angiography demonstrated bilateral ICA stenosis (figure 1: A,B), initially reported as acute bilateral dissection. Subsequent MR angiographic imaging revealed dynamic changes in left ICA stenosis (figure 1: C,D). Repeat CT angiogram 1 month later showed patent carotids bilaterally (figure 1: E,F). A diagnosis of recurrent ICA vasospasm was made. Multiple vasodilatory treatments were trialled without success in preventing future episodes. She underwent unilateral thoracic sympathectomy of the most symptomatic side, with initial prolonged resolution of events. Subsequent recurrent events have been treated with corticosteroids.
Conclusions:: Spontaneous vasospasm of the extracranial ICA has been rarely reported as a cause of stroke. Diagnosis is reliant on early and repeated angiographic studies. The pathophysiology has been postulated to be migraineous, or related to ICA sympathetic hypersensitivity. Optimal management remains uncertain for this rare condition.
A PRIMARY STUDY OF TRPM2 ON SH-SY5Y CELL INJURY AFTER OGD/R

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Background and Aims:: The role of TRPM2 in cerebral ischemia/ reperfusion (I/R) injury is gaining increasing attention in research, but the underline mechanism remains unclear. The purpose of our study was to investigate the role of TRPM2 in SH-SY5Y cell injury induced by I/R and its time points of effect.

Methods:: SH-SY5Y cells were subjected to oxygen-glucose deprivation/reperfusion (OGD/R) to mimic cerebral I/R injury in vitro. Cell morphology, viability and apoptosis were detected by histology, Cell Counting Kit-8 assay and flow cytometry, respectively at different time points after OGD/R. Expression of TRPM2 were measured by quantitative real-time PCR and Western blotting analysis.

Results:: Our data showed that SH-SY5Y cell viability was significantly decreased at OGD 6h (P<0.05). Cell viability was the lowest at OGD6h/R3h (P<0.05). Cell apoptosis rate increased the most at OGD 6h (P<0.05). After reperfusion, cell apoptosis rate was the highest at OGD6h/R3h (P<0.05). The expression level of TRPM2 reached its peak at OGD 6h. TRPM2 was positively correlated with cell apoptosis rate (r=0.9114, P<0.05), and was negatively correlated with cell viability (r=-0.9973, P<0.05) within OGD6h. During reperfusion, TRPM2 was positively correlated with cell apoptosis rate (r=0.9947, P<0.05), and was negatively correlated with cell viability (r=-0.9361, P<0.05) within R3h. Parallelly, TRPM2 gene and protein expression were the highest at OGD 6h/ R 3h (P<0.05).
Conclusions:: TRPM2 expression was upregulated in OGD/R conditions with peak at OGD6h/R3h. TRPM2 was positively correlated with cell apoptosis within R3h. We speculate that TRPM2 may play a key role in delayed cell injury caused by OGD/R.
USE OF NON-CONTRAST ENHANCED T1-WEIGHTED THREE-DIMENSIONAL FAST-SPIN ECHO IMAGING FOR THE EVALUATION OF INTRACRANIAL VASCULAR STENT PLACEMENT

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Gunma University Graduate School of Medicine, Department Of Neurosurgery, Maebashi, Gunma, Japan

Background and Aims:: Evaluation of intracranial stent placement by magnetic resonance imaging suffers the problems of signal artifacts during time-of-flight magnetic resonance angiography (TOF-MRA). Therefore, angiographic examination is required for detailed intravascular assessment of the stent placement site. Recently, three-dimensional T1-turbo spin echo (3D-TSE) has been developed for evaluation of carotid artery stent placement. We investigated the use of the 3D-TSE imaging method for the evaluation of intracranial vascular stent placement.

Methods:: The subjects consisted of nine patients who underwent intracranial vascular stent placement from April 2015 and December 2019. Postoperatively, the lumens of the placed stents were measured by TOF-MRA, digital subtraction angiography (DSA), and 3D-TSE imaging. Analysis was performed by type of stent and placement site.

Results:: The stents used were Neuroform Atlas (3 patients), LVIS (3 patients), LVIS Jr (2 patients), and Integrity (1 patient). TOF-MRA of the stent placement site showed defects in the image or poor visualization in all nine patients, whereas 3D-TSE imaging visualized the lumen at the stent indwelling site in all patients. The blood vessel diameter measured by the DSA and 3D-TSE imaging exhibited positive correlations regardless of the stent type and placement site.

Conclusions:: 3D-TSE imaging allows visualization of the lumen of the site of an intracranial vascular stent, regardless of the type of stent or the vessel. Thus, this method may be useful for evaluating the vascular lumen of a lesion.
Background and Aims:: Neurological complications of the peripheral nervous system are frequent in people living with HIV and neuromuscular pathology is associated with significant morbidity. The purpose of this study was to describe the clinical profile of people living with HIV suffering from peripheral neuropathy (PN) in Lubumbashi, Democratic Republic of Congo.

Methods:: This is a cross-sectional study at the Centre d’Excellence VIH/Sida of the University of Lubumbashi for a period of one year. A total of 101 people living with HIV were selected. Our analysis was essentially clinical. To refine the diagnosis, we used the DN4 Assessment Tool (diagnosis of neuropathic pain) and the Visual Analogue Scale (evaluation of the severity of pain).

Results:: Of a total of 3237 people living with HIV followed, 101 presented the PN, a prevalence of 3.12%. 53.3% of patients had an abolition of the deep tendon reflexes of the lower limbs and 77.89% have a ‘socks and gloves’ hypoesthesia. 80% of patients consulted for pains of lower limbs, 25% presented an amyotrophy of the lower limbs and about 3.6% have a real difficulty to walk. The totality of the patients had a score greater than or equal to 5 out of 10 at the Visual Analogue Scale. The assessment of neuropathic pain using the DN4 Assessment Tool showed that 94.5% of patients had a score greater than or equal to 4.

Conclusions:: The PN alters the quality of life of people living with HIV and decreases adhesion to antiretroviral therapy.
Efficacy and Safety of Eculizumab in Patients with Treatment-Refractory Anti-Acetylcholine Receptor Antibody-Positive Generalised Myasthenia Gravis Previously Treated with Rituximab

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Background and Aims:: The phase 3 REGAIN study (NCT01997229) and its open-label extension (OLE; NCT02301624) evaluated eculizumab’s efficacy and safety in patients with anti-acetylcholine receptor antibody-positive refractory generalised myasthenia gravis (gMG). Although not approved for MG, rituximab has been used in such patients. The aim of this secondary analysis was to assess response to eculizumab in individuals with gMG previously treated with rituximab. Eculizumab is not reimbursed for neurology indications in Italy as of April 2021.

Methods:: Baseline disease characteristics, safety and response to eculizumab were compared in patients who had previously received rituximab (prior-rituximab group) and those who were rituximab naïve. Rituximab was prohibited within 6 months before screening or during REGAIN/OLE.

Results:: Of 125 patients, 14 had previously received rituximab (placebo, n=7; eculizumab, n=7). Patients with and without rituximab exposure had comparable mean baseline MG-Activities of Daily Living (MG-ADL) total scores (10.6 vs 10.1) (Table 1). A higher proportion of patients in the prior-rituximab group had used ≥4 immunosuppressants (57.1% vs 16.2%) (Table 1). Patients who had received 18 months’ eculizumab treatment experienced similar clinical improvements, regardless of previous rituximab administration (mean [standard deviation] change in MG-ADL total score from REGAIN baseline to OLE week 52, −3.8 [3.54] in prior-rituximab group [n=6] and −5.3 [3.49] in rituximab-naïve patients [n=43]). Eculizumab safety was consistent with its known profile.
Conclusions:: Although patients in the prior-rituximab group had more refractory disease, they experienced similar long-term clinical improvement with eculizumab to rituximab-naïve patients. Updated data will be presented. This study was funded by Alexion Pharmaceuticals, Inc.

Table 1. Patient characteristics and MG-ADL total scores at REGAIN baseline

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Prior rituximab (n=14)</th>
<th>No prior rituximab (n=111)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>12 (85.7)</td>
<td>70 (63.1)</td>
</tr>
<tr>
<td>Male</td>
<td>2 (14.3)</td>
<td>41 (36.9)</td>
</tr>
<tr>
<td>MG history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at MG diagnosis, years, mean (SD)</td>
<td>27.6 (14.8)</td>
<td>39.4 (18.7)</td>
</tr>
<tr>
<td>Duration of MG, years, mean (SD)</td>
<td>13.9 (10.5)</td>
<td>9.0 (7.8)</td>
</tr>
<tr>
<td>Time to gMG if first clinical presentation was oMG, months, mean (SD)</td>
<td>5.1 (6.6)</td>
<td>16.3 (31.6)</td>
</tr>
<tr>
<td>Treatment history, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Used only two ISTs</td>
<td>1 (7.1)</td>
<td>57 (51.4)</td>
</tr>
<tr>
<td>Used only three ISTs</td>
<td>5 (35.7)</td>
<td>34 (30.6)</td>
</tr>
<tr>
<td>Used at least four ISTs</td>
<td>8 (57.1)</td>
<td>18 (16.2)</td>
</tr>
<tr>
<td>Used IVlg</td>
<td>14 (100.0)</td>
<td>85 (76.6)</td>
</tr>
<tr>
<td>Used PLEX</td>
<td>9 (64.3)</td>
<td>51 (45.9)</td>
</tr>
<tr>
<td>Baseline MG-ADL total score, mean (SD)</td>
<td>10.6 (3.48)</td>
<td>10.1 (2.76)</td>
</tr>
</tbody>
</table>

gMG, generalised myasthenia gravis; IST, immunosuppressive therapy; IVlg, intravenous immunoglobulin; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis-Activities of Daily Living; oMG, ocular myasthenia gravis; PLEX, plasma exchange; SD, standard deviation.
ESTIMATION OF MYASTHENIA GRAVIS PREVALENCE IN ITALY USING REAL-WORLD DATA

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Background and Aims:: Few data are available regarding the epidemiology of Myasthenia Gravis (MG) in Italy during the most recent years. The study aims to evaluate the MG prevalence in a real-world setting and to estimate the number of patients currently living with MG in Italy.

Methods:: We conducted an observational retrospective study based on administrative databases covering around 11.4 million subjects across Italy. Patients were included between 01/2011-12/2018 (inclusion period) by hospitalization discharge diagnosis for MG, or by active exemption code for MG or by presence of ≥1 pyridostigmine prescription. Prevalence was calculated on patients alive at 01/01/2018 and stratified by gender. Data were reproportioned to the Italian Population.

Results:: From preliminary data, we identified 4,078 MG patients (mean age 61.3 years, 46.2% male), mostly by pyridostigmine prescription (72%), followed by exemption code (15%) and hospitalizations (13%). Among the latter, 65.8% was hospitalized for MG without exacerbation, 33.8% with exacerbation. MG prevalence was 28.9 patients per 100,000 subjects (27.1 cases per 100,000 males, 30.6 cases per 100,000 females) (Figure 1). Data projected to the Italian population estimated a total of 17,480 patients (7,972 males and 9,508 females) affected by MG.

Conclusions:: Preliminary results show an MG prevalence at 01/01/2018 of 28.9 patients per 100,000 subjects, slightly higher compared to previous Italian studies. However, our study is consistent with recent evidence suggesting an increase in MG prevalence. We estimate 17,480 MG patients in Italy, which is in line with current estimates of 15,000-20,000 MG patients.
LAMBERT EATON MYASTHENIC SYNDROME MASQUERADING AS MYOPATHY IN ASYMPTOMATIC LUNG MALIGNANCY

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Background and Aims:: Introduction: Lambert-Eaton Myasthenic Syndrome (LEMS), is a rare disorder characterized by antibodies against presynaptic voltage-gated calcium channels in the neuromuscular junction. It is regarded as a paraneoplastic syndrome, as most patients have an underlying malignancy, commonly a small-cell lung cancer (SCLC).

Methods:: Case Presentation: 59-year-old Malay male, a 30 pack-year smoker with no past medical history, presented with 3-week history of progressive proximal weakness affecting ambulation, lethargy, and dry mouth with no respiratory complaints or constitutional symptoms. Examination revealed proximal weakness, global hyporeflexia, and waddling gait. Significant incremental response with high-frequency repetitive nerve stimulation (RNS) suggested a presynaptic neuromuscular junction disorder. CT Thorax revealed a 3cm right lung mass with biopsy confirming small-cell carcinoma. Anti-Voltage-gated Calcium-channel antibody was positive. He received intravenous Immunoglobulin therapy and 3,4-diaminopyridine for LEMS, chemotherapy for malignancy, and rehabilitation. During follow-up visits, he showed marked improvement.

Results:: Discussion: LEMS is a complex and rare paraneoplastic syndrome that presents with proximal muscle weakness, hyporeflexia, and autonomic disturbances. LEMS is more common in males with smoking being a known major risk factor for lung cancer. LEMS is predominantly associated with SCLC and in gastric cancer, lymphosarcoma, malignant thymoma, breast & colon cancer. Cornerstone of diagnosis is clinical suspicion with nerve conduction studies and Anti-Voltage-gated Calcium-channel antibodies which are pathognomonic for LEMS.

Conclusions:: While evaluating proximal muscle weakness, paraneoplastic syndrome LEMS as a cause should be suspected, even without respiratory or constitutional symptoms, especially in smokers. RNS to confirm LEMS and malignancy screening would enable early pathohistological-detection and treatment of underlying cancer.
Background and Aims:: Myasthenic crisis (MC) affects 15-20% of patients with myasthenia gravis (MG), requiring mechanical ventilation (MV) and intensive care unit (ICU) assistance. Patients may develop more than one crisis during life. Aim of the study was to assess whether patients with multiple MC have a worse prognosis.

Methods:: We identified 90 patients referred to Neurology Department in Modena presenting MC between January 2000 and September 2020.

Results:: Out of 90 patients, 29 cases (32%) had more than one episode of MC, ranging from 2 (20 patients) to 4 episodes (2 patients). In the group of patients with multiple MC, 18 (62%) were females and 17 (59%) had a late onset MG. Anti-AChR antibodies were detected in 24 (83%) and one exhibited anti-MUsK antibodies. There were no significant differences between patients with one or more MC in respect of gender, age at onset or anti-AChR-Ab titer at baseline, whereas patients with recurring MC were significantly more affected by multiple (>3) comorbidities (p=0.04). Fifty per cent of patients with relapsing MC needed invasive MV. Patients with multiple MC did not show higher risk for need of MV or tracheostomy due to weaning failure, whereas they exhibited significantly longer than 7 days ICU stay (p=0.01). Out of the 4 deaths for MC, 3 patients had more than one MC.

Conclusions:: MG patients with more than one MC do not exhibit higher risk of MV or tracheostomy, but they may be at risk of longer ICU stay.
AN UNUSUAL CASE OF BULBAR PALSY PLUS/ASMAN OVERLAP

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Background and Aims:: Bulbar palsy plus (BPp) is a variant of Guillain Barré syndrome (GBS), characterized by bulbar symptoms and others cranial nerves deficits or ataxia, without limbs or neck weakness, usually associated with presence of GQ1b and G11a antibodies.

Methods:: We describe a case of BPp overlapped by a sensory-motor axonal neuropathy (ASMAN).

Results:: A 62 years old man, without relevant medical history, was admitted to Emergency Room for dysphagia, voice reduction and paraesthesia to distal extremities started 4 days earlier, after a diarrhoeic episode. Neurological examination showed absent tendon reflexes, mild ophthalmoparesis and asymmetrical palpebral ptosis. Cerebrospinal fluid (CSF) analysis and neurophysiological study (NPS) were normal, showing only absent H reflex. Repetitive nerve stimulation at low and high frequencies was normal. Intravenous immunoglobulins 0.4 gr/kg die for 5 days were started. Subsequently he developed tetra-hyposthenia and worsening of bulbar function, complete gaze palsy and bilateral ptosis, requiring mechanical ventilation and nasogastric tube. 15 days after symptoms onset, CSF analysis showed albuminocytological dissociation and NPS showed diffuse sensory-motor axonal neuropathy. Initially no serum anti ganglioside were detected, but 15 days after GT1a, Gq1b, GD2 and GD3 IgG were positive. RT-PCR and serology for SARS-COV 2 were negative. Campylobacter search was negative. About 15 days after onset he started recovery and at 50 days he was discharged from rehabilitative ward.

Conclusions:: BPp is recently recognised as a rare GBS variant, such as Miller Fisher syndrome (MFS) or pharyngeal-cervical-brachial (PCB) variant. Overlap between AMSAN and the other variants was already described. This is an interesting case of BPp/ASMAN overlap syndrome.
NXP2-POSITIVE DERMATOMYOSITIS: A CHALLENGING SUBGROUP OF INFLAMMATORY MYOPATHIES

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Background and Aims:: Dermatomyositis (DM) represents an idiopathic inflammatory disorder with distinctive skin and muscle involvement. NXP2 (Nuclear Matrix Protein) antibodies positivity defines an uncommon subgroup of patients, with variable clinical outcomes.

Methods:: We describe four cases of NXP2 positive DM diagnosed at Neuromuscular Centre in Torino (Italy), with a long-term follow up (up to 5 years). Age of patients ranged from 30 to 69 years; all of them had a severe clinical involvement, with proximal muscle weakness, marked persistent skin involvement and high CK levels.

Results:: A 46-year-old man with severe persistent generalized weakness and dysphagia, requiring percutaneous nutrition, showed a good response to Rituximab therapy, after multiple steroids, IVIG, Methotrexate and Azathioprine unsuccessful trials. A 69-year-old woman with extended multifocal areas of myositis ossificans with intolerance to steroid therapy reached a good control of clinical manifestations after repeated courses of Rituximab. A 30-year-old woman diagnosed with dermatomyositis and lupus panniculitis is now in remission with Azathioprine and low doses of Prednisone after several trials of higher doses of steroids, Methotrexate and Mycophenolate; lastly, a 56-year-old woman with a predominant cutaneous dermatomyositis had a sustained improvement with oral Prednisone and Azathioprine.

Conclusions:: In the NPX2 positive subgroup of DM we observed a clinical course generally more severe than in other DM cases, especially for skin and subcutaneous involvement. In three out of four patients the combination of multiple immunomodulatory agents was necessary to obtain a remission; in two of them only Rituximab therapy caused a remission.
CASE REPORT OF SOD1 ALS PRESENTING WITH PROMINENT HEARING IMPAIEMENT

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Background and Aims:: Amyotrophic lateral sclerosis is the neurodegenerative disease involving both upper and lower motor neurons. Familial amyotrophic lateral sclerosis (fALS) accounts for almost 10% of all cases of ALS. It is a gradually progressive disease with duration of more than 10 years and occurrence of atypical features such as pain, paraesthesia or urgency micturition. In case of ALS presenting with deafness, riboflavinopathies and madras motor neuron disease must be suspected from Indian subcontinent. Evaluating for ALS genes is important as SOD1 mutation can present with predominant deafness.

Methods:: A 44 year old female born out of nonconsanguineous marriage with 2 years history of decreased hearing and 1 year history of progressive bulbar complaints in form of episodes of choking and nasal regurgitation with spastic dysarthria. She had asymmetric weakness affecting upper limbs distal followed by proximal. On examination there was thinning noticed predominantly affecting thenar muscles, forearm extensors and triceps and biceps. Profuse fasciculations, spasticity with brisk reflexes and upgoing plantar was noticed involving all four limbs. Spastic dysarthria with tongue atrophy with prominent fasciculations were seen.

Results:: Electrophysiological studies were suggestive of active and chronic denervation affecting cervical, thoracic and bulbar segments. Pure tone audiometry showed bilateral sensorineural hearing loss. Paraneoplastic and other secondary causes were ruled out. Exome panel revealed missense mutation in exon 3 of SOD1 gene which was reported to be pathogenic.

Conclusions:: This case highlights that SOD 1 mutation ALS should be considered in differential diagnosis of patients presenting with progressive hearing loss with bulbar onset ALS.
LGMD LIKE PRESENTATION OF MARINESCO SJOGREN SYNDROME: ATYPICAL PRESENTATION OF RARE DISEASE

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Background and Aims:: Marinesco-sjogren syndrome is a rare, autosomal recessive disorder. Mutation in SIL-1 gene account for majority of cases. It commonly presents with cerebellar ataxia, congenital cataracts, myopathy and mental retardation. Skeletal abnormalities including short stature, dysarthria, nystagmus and hypergonadotropic hypogonadism are also occasionally observed. Myopathic presentation without ataxia is rare. We are reporting this rare LGMD like presentation of genetically proven marinesco sjogren syndrome as it is probably the first case report after thorough review of literature.

Methods:: A 26-year-old female born out of non-consanguineous marriage, presented with purely motor symmetrical predominantly limb-girdle weakness started at the age of 11-12 years without any history of ataxia. She was operated for bilateral cataracts at 3 years of age and had primary amenorrhea. Birth and developmental history revealed delayed cry and mild delayed motor milestones. Family history revealed history cataract surgery at age of 6 year with limb-girdle weakness in 2nd elder sister. General examination showed microcephaly. Neurological examination showed hypotonia, proximal more than distal weakness in all the four limbs with preserved deep tendon jerks. Cerebellar signs were absent.

Results:: On evaluation, Serum creatine kinase was elevated, electrophysiology showed myopathic units, and IQ was 69 %. FSH, LH were elevated and MRI brain showed mild cerebellar atrophy. Genetic studies showed homozygous mutation in SIL-1 gene at exome 3 which was consistent with marinesco-sjogren syndrome.

Conclusions:: This case highlights that Marinesco-sjogren syndrome should be considered in differential diagnosis of patients presenting with LGMD phenotype, cataracts and hypergonadotropic hypogonadism even without ataxia.
REST OR 30 MIN WALK AS EXERCISE INTERVENTION (RESTOREX) IN MYASTHENIA GRAVIS: A RANDOMIZED CONTROLLED TRIAL

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Background and Aims:: There is lack of evidence about the usefulness of exercise or rest in myasthenia Gravois (MG). The study is aimed to evaluate the efficacy and safety of exercise or rest in MG.

Methods:: In a single center open labeled randomized controlled trial, the patients with mild to moderate MG were randomized to 30 minute walk or rest in addition to the standard treatment. The primary endpoint was 50% improvement in the MG Quality of Life (MG-QOL15), and secondary endpoints were change in the Myasthenic Muscle Score (MMS), MG Activities of Daily Living (MGADL), grip strength, dose of acetylcholine esterase inhibitor and prednisone, 6 minute walk test (6MWT), decrement in trapezius on low rate repetitive nerve stimulation test and adverse events. The outcomes were defined at three months, by more than 50% improvement in these outcome parameters.

Results:: Forty patients with MG were randomized to exercise or rest arm. The two arms were matched for demographic and clinical parameters. The patients in the exercise arm had significantly better QOL evidenced by MG-QOL15 (P=0.02). The secondary end points, distance covered in 6MWT (P=0.007) was also better in the exercise arm without any adverse event.

Conclusions:: Regular exercise for 30 min in mild and moderate MG improves quality of life and walking distance compared to rest, and is safe.
PATISIRAN IN HATTR AMYLOIDOSIS: 6 MONTHS LATENCY BEFORE EFFICACY

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Background and Aims:: Hereditary amyloidosis associated with mutations in the transthyretin gene (hATTR) is a progressive devastating disease, with fatal outcome occurring within ten years after onset. In recent years, TTR gene silencing therapy appeared as a promising therapeutic strategy, showing evidence that disease progression can be slowed and perhaps reversed.

Methods:: We report here 18 subjects affected by hATTR amyloidosis treated with patisiran, a small interfering RNA acting as TTR silencer, and evaluated with PND score, NIS and NIS-LL scale, and Norfolk QOL-DN questionnaire at baseline and then every 6 months.

Results:: A global clinical stabilization was observed for the majority of the patients, with mild-moderate improvements in some cases, even in advanced disease stage (PND score >2).

Conclusions:: Analysis of NIS, NIS-LL and Norfolk QOL-DN results and PND score variation suggest the possible presence of a 6-month latency period prior to benefit of treatment becomes evident.
GENOTYPE-PHENOTYPE CORRELATION IN FSHD-LIKE PATIENTS WITH UNCOMMON FEATURES

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Background and Aims:: Since the first descriptions of the FSHD phenotype, an interesting range of uncommon features have been described. This clinical variability is captured by the Comprehensive Clinical Evaluation Form (CCEF). We investigate the genotype-phenotype correlation in FSHD-like patients (D1 patients on the basis of CCEF) and the distribution of clinical categories in D1 families.

Methods:: The study was performed on the subjects accrued through the Italian National Registry for FSHD (INRF), from January 2016 to October 2019. The cohort selected includes all subjects, carrying or not a D4Z4 allele of reduced size, assessed with clinical category D1.

Results:: We identified 198 D1 subjects (101 females), 176 were probands and 22 relatives. Mean age at onset was 39.8; mean FSHD score was 6.2 (SD 2.8) in probands and 5.3 (SD 2.7) in relatives (p value = 0.2128) and no significant differences were detected between males and women in FSHD score. No particular size of DRA prevails among subjects assessed with category D1. No significant clustering of any uncommon feature was found. 61.3% of the relatives of D1 patients were asymptomatic (category C).

Conclusions:: D1 subjects are myopathic subjects with the co-presence of genetic and environmental factors and the D4Z4 reduced allele may be one of the various factors contributing at the clinical picture. The probability for relatives of D1 probands to develop a myopathic phenotype is low. This observation is highly relevant for clinical management because additional parameters to be used in clinical practice for diagnosis ad interpretation of the clinical phenotype.
THE LIGHT AT THE END OF THE TUNNEL: MNGIE BETWEEN LIVER TRANSPLANTATION AND BONE MARROW TRANSPLANT.

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Background and Aims:: Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) an autosomal recessive disease caused by loss-of-function mutations in the nuclear gene coding for the cytosolic enzyme thymidine phosphorylase. New Research that has been published in the past few years are recommending more and more that HSCT and liver transplantation is a therapy of choice if the patient is found early and has no complications to eliminate MNGIE's manifestations and provide our patients with a quality of their lives. Here we review the literature and efforts done to further prove the efficacy and safety of transplantation (whether bone marrow or liver) for MNGIE condition.

Methods:: A systemic review through the databases of Pubmed and Google Scholar (articles selected for the review/articles found on pubmed: 19); Bone marrow Transplantation 13/19 AND Liver Transplantation 6/19.

Results:: Review of cases that had the opportunity to receive either a bone marrow or liver transplant prior to 2010 were unfortunately presenting late and in poor medical condition or were not in the most optimal transplant conditions that are available with today's quality of care and transplantation services and breakthroughs. Newer published cases prove that improvement of the transplantation process and care shows promising results. However, it is too early to judge with the short follow up dates.

Conclusions:: The limited number of published cases and the expert opinions regarding the bone marrow and liver transplantation as a potential management for MNGIE proves to be a frontier worth looking into and advancing the limits of management provided to our patients.
A CASE OF LATE ONSET SEVERE NEUROLOGICAL IMMUNE-RELATED TOXICITY DUE TO
NIVOLUMAB TREATMENT IN A PATIENT WITH METASTATIC MELANOMA

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Background and Aims:: Even though rare, neurological immune-related toxicity due to immune checkpoint inhibitors (ICIs) therapy (e.g. Nivolumab) is described¹. We report an uncommon case of late-onset Nivolumab-related neurological toxicity.

Methods:: A 65-year-old woman was diagnosed with metastatic melanoma and treated with Nivolumab with full remission. After three years of treatment, she reported subacute distal lower limbs paresthesia and hypopallesthesia, followed by progressive paraparesis, dysautonomic failure (severe hypotension, bradycardia episodes), monolateral facial nerve’s peripheral palsy, visual impairment and fluctuating diplopia. Her clinical history was relevant for previous HCV-hepatitis.

Results:: The following investigations were performed. (1)EMG/ENG/SFEMG/RNS/SSR: severe demyelinating multifocal sensory-motor and dysautonomic polyneuropathy with cranial involvement; increased jitters, pathological blocks; (2)VEP: abnormalities bilaterally; (3)Brain/spinal cord MRI: no relevant outcomes; (4)CSF: albumin-cytologic dissociation and rare lymphocytes; (5)Anti-AChR antibodies: absent. (6)Biochemical investigations (anti-onconeural antigens and anti-ganglionic AchR antibodies, diabetes, autoimmune screening, infectious diseases) were unremarkable. (7)Instrumental tests excluded oncological relapse or myositis. Corticosteroid oral treatment generated no benefits. Plasmapheresis led to an initial clinical stabilization, followed by a relapse. An overall neurophysiological and clinical improvement was obtained with IGIV.

Conclusions:: Immune-related adverse events due to ICIs, including neuromuscular disorders (MG, myositis, GBS, CIDP), usually occur after 3-6 months of therapy¹. Our case presented an unusual late onset. This case is characterized by multifocal demyelinating polyneuropathy with associated dysautonomic component (rarely described before²) and concomitant signs of neuromuscular junction disorder. Neuromuscular disorders should be considered when deciding for starting ICIs administration. A prompt diagnosis is essential to set up an effective immunomodulant therapy. ¹Möhn-et-al-Journal-of-Clinical-Medicine-(2019),8,1777;https://doi:10.3390/jcm8111777 ²Gao-et-al-Journal-for-Immuno-Therapy-of-Cancer-(2019),7,262;https://doi.org/10.1186/s40425-019-0748-0
COGNITIVE FUNCTION ASSESSMENT IN PATIENTS WITH MYOTONIC DYSTROPHY TYPE 2

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Background and Aims:: Myotonic dystrophy type 2 (DM2) is an autosomal dominant, slowly progressive, multisystemic, late-onset disease. Previous research showed impaired cognitive function in DM2. The aim of our study was to assess cognitive functions and the presence of dementia in a large cohort of DM2 patients using an extensive battery of neuropsychological tests.

Methods:: The study included 76 patients with genetically confirmed DM2. Raven Standard Progressive Matrices (RSPM) were used to assess general intellectual level. MMSE and Addenbrooke’s tests were used as a cognitive screening. Patients underwent neuropsychological testing in following domains: memory, language, attention, executive and visuospatial functions.

Results:: Only 6% of DM2 patients achieved a below-average score on RSPM. The presence of cognitive decline was found in 6% of patients according to MMSE and 26% of patients according to ACE-R. Regarding individual neuropsychological domains, the worst results were observed in the visuospatial and language areas with around 50% of patients being one standard deviation below the norm, followed by executive dysfunction. Twenty (26%) patients had impairment of at least 2SD below the norm on at least 2 tests from 2 different domains. Even more, fifteen (20%) patients and their relatives reported a significant impact of cognition on daily activities. Age at testing and at disease onset, education, and muscle weakness correlated with cognitive findings.

Conclusions:: DM2 patients frequently had visuospatial, language, and executive function impairments, while the general intellectual level was preserved. One-fifth of patients had signs of dementia.
A NERVE METASTASIS IN THE BRACHIAL PLEXUS

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Background and Aims:: Cancer rarely metastasizes into peripheral nerves. Increasingly imaging and in particular ultrasound allow a precise diagnosis.

Methods:: A tumorous growth was found in the brachial plexus of the body of a patient with a known breast cancer. Body donation to the anatomic institute is the basis of ongoing anatomical studies. Persons can be identified by name, and age, but clinical data are not available. This is why a classical „case report“ is not available. The brachial plexus was examined anatomically by HR nerve ultrasound. Neuropathological examination of the tissue, including immunohistochemistry was performed at the Institute of neurology, of the university of Vienna.

Results:: The exact site of nerve enlargement could be documented by ultrasound, Histology confirmed a local nerve metastasis in the proximal parts of the median nerve, arising from the brachial plexus. Neuropathology showed epi- and perineurial cancer infiltration, compatible with breast cancer (cytokeratin and GATA-3 positive) . Tumorous enlargement of cranial and peripheral nerves in malignancy are caused lymphoma, leukemia, cancer and other malignancies. Peripheral nerve involvement in malignancies ranges from compression to focal invasion, to different types of parenchymatose involvement, which can be diffuse, intra- or extrafascicularly, in the vessel, around the vessel or as a solid metastatic growth. Epineurial and paraepineurial spread can appear. The frequency of nerve metastasis often are underestimated.

Conclusions:: This is a rare observation. Despite the absence of clinical data the identification with HD ultrasound, anatomical preparation and histological evaluation allows a comparison of the evaluation of structures by different methods.
CARPAL TUNNEL SYNDROME: FACTORS INTERFERING WITH THE SURGICAL RESPONSE AND THE SATISFACTION DEGREE OF THE OPERATED PATIENT

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Background and Aims:: The Carpal Tunnel Syndrome (CTS) is the most common compressive mononeuropathy of the upper limbs. Nervous compression may cause functional and motor injuries. The surgical intervention is a highly effective therapeutic option. The aim of this study was to evaluate factors that interfere in the surgical response and the degree of postoperative satisfaction.

Methods:: This research was approved by the Ethics Research Committee (48320815.1.0000.5553). We evaluated 74 patients who underwent surgery for CTS. Factors such as sex, age, body mass index, occupation, comorbidities, lifestyle, and surgical response were studied. If the symptoms persist, the patient’s satisfaction degree was assessed, categorized as dissatisfied and unresponsive to treatment.

Results:: Sixty-eight were women. Mean age of the patients was 48 years. Twenty-three patients were obese. Thirty-one were homemakers or manual workers. Of the 67 patients evaluated, 48 (71.64%) were dissatisfied and categorized as not responding to surgical treatment. Linear regression analysis identified that alcoholism, at the time of surgery, was a significant factor, leading to 3.5 times more complications than in the non-alcoholic group (p = 0.05). In the smoking group, the complication rate was 1.2 times lower (p = 0.1). Other variables studied did not interfere with the surgical response.

Conclusions:: Most patients were categorized as dissatisfied and unresponsive to surgical treatment. The alcoholism was the only factor identified as relevant to the increase in complications. Paradoxically, smoking was configured as a protective factor, which may reflect a bias in the sample selection.
DERMATOMYOSITIS WITH SUPERIMPOSED COVID-19 MYOSITIS

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Background and Aims:: Background and aims: Covid-19 pandemic has the potential to modify the presentation of neuromuscular disorders. We describe one such patient who had COVID-19 infection along with dermatomyositis. He had typical rash and muscle weakness but also had rhabdomyolysis at presentation and muscle biopsy showed necrotic muscle fibres. He was treated with intravenous steroids and rituximab and showed gradual recovery.

Methods:: We present a case of 16 year old male who presented to us with bodyaches, myalgia, proximal muscle weakness, rash over face and limbs along with fever for 1 month duration. We examined him clinically, investigated accordingly and performed muscle biopsy.

Results:: On clinical examination he had typical rash of dermatomyositis with heliotrope eruption and gottron papules along with proximal muscle weakness, neck and truncal weakness with preserved deep tendon reflexes. CK-NAC was elevated and urine myoglobin was present. EMG was suggestive of myopathic illness and anti Mi-2 beta was positive. Muscle biopsy showed multiple necrotic fibres without increase in inflammatory infiltrate. Intravenous steroids followed by oral steroids along with rituximab was given and he recovered gradually.

Conclusions:: COVID-19 can alter clinical presentation, histopathological findings and prognosis of neuromuscular diseases. We must be cautious in interpretation during ongoing COVID-19 pandemic.
THE INCIDENCE OF MYASTHENIA GRAVIS IN THE REPUBLIC OF MOLDOVA BEFORE AND DURING THE COVID-19 PANDEMIC

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Background and Aims:: The aim of this study is to provide an estimated incidence of Myasthenia Gravis (MG) and to describe the pattern of the disease in the Republic of Moldova before and during the COVID-19 pandemic.

Methods:: Multiple sources of cases were explored prospectively and retrospectively during a nationwide study of MG in the Republic of Moldova. The date the SARS-CoV-2 infection (11 March 2020) was declared a pandemic was used as a reference and the clinical features of the new (incident) cases ascertained one year before and one year after that date were compared.

Results:: During the period 11 March 2020 - 11 March 2021, 28 new cases of MG were ascertained yielding a crude incidence rate of 10.6 per million person-years (95% CI 6.7-14.5), 13.1 in women (95% CI 7.1-19.1) and 7.8 in men (95% CI 3-12.6) (F:M ratio of 1.6:1). The mean age of onset was 49.8 years (43.2 in women and 62.7 in men). Only 5 thymectomies were performed. During 11 March 2019 - 10 March 2020, 35 new cases of MG were identified yielding a crude incidence rate of 13.0 per million person-years (95% CI 8.7-17.3), 14.9 in women (95% CI 8.6-21.2) and 10.9 in men (95% CI 5.2-16.6), (F:M ratio of 1.3:1). The mean age of onset was 48.3 years (47.1 in women and 57.2 in men). 17 thymectomies were performed.

Conclusions:: During the COVID-19 pandemic, the incidence of MG was slightly lower than the previous year. This could be due to the fact that patient management and hospital care have been markedly impacted.
REPETITIVE NERVE STIMULATION TEST IN PATIENTS WITH MYASTHENIA GRAVIS

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**Background and Aims:** Myasthenia gravis (MG) is a rare and an autoimmune disease mainly caused by antibodies against the acetylcholine receptor on the postsynaptic membrane at the neuromuscular junction. Localized or generalized muscle weakness is the predominant symptoms. Repetitive nerve stimulation (RNS) confirms diminished neuromuscular transmission. We aimed to study the RNS test in myasthenic patients in Mongolia.

**Methods:** We retrospectively reviewed collected data obtained from myasthenic patients who have undergone examination at our clinic between January, 2016 and February, 2021. RNS test results were also recorded based on electrodiagnostic reports at the time of initial visit to our clinic. We made RNS test in muscles of facialis, accessorius, medianus, and peroneus nerves. A decrement in compound muscle action potential amplitude of ≥10% was considered abnormal. Statistical analysis was performed by using the SPSS, version 21.

**Results:** We surveyed 50 patients with MG; 31 (62.0%) were females and 19 (38.0%) were males. Overall mean age was 35.45±17.74 years (range 2-72). The abnormal response of the amplitude of the compound muscle action potentials was 94.0% in nasalis muscles, 88.0% in trapezius muscles, 58.0% in abductor pollicis brevis muscles and 56.0% in extensor digitorium brevis muscles. RNS test abnormality of abductor pollicis brevis (p=0.003) and extensor digitorium brevis (p=0.003) muscles were significantly associated with generalized MG.

**Conclusions:** RNS test is important role to identify MG in a majority of patients.
AN UNUSUAL PHENOTYPE OF RECESSIVE CONGENITAL MYOPATHY: EXPANDING THE SPECTRUM OF ORAI-1 ASSOCIATED DISORDERS.

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Background and Aims:: The primary storehouse of the intracellular calcium ions, which play a crucial role in the excitation-contraction of skeletal muscles, is the sarcoplasmic reticulum. Calcium flux is mediated by the store-operated Ca2+ entry (SOCE) pathway interacting with stromal interacting molecule 1 (STIM-1), an SR calcium sensor, and ORAI-1, a plasma membrane calcium release-activated channel (CRAC). Loss of function mutation of ORAI-1 causes severe combined immunodeficiency (SCID), non-progressive muscle hypotonia, and anhidrotic ectodermal dysplasia. Autosomal dominant gain of function mutation causes syndromic and non-syndromic tubular aggregate myopathy. Here we report a unique case of homozygous ORAI-1 mutation presenting clinically as congenital myopathy and histologically as Congenital fibre type disproportion (CFTD).

Methods:: An 18 years old female presented with two and a half years history of progressive pain in both thighs followed by weakness of proximal lower limbs. She has squint in both eyes along with difficulty in running since childhood. The patient was thin built along with long facies. There was hypotonia of lower limbs along with muscle power of 4 in upper limbs and 3 in lower limbs. She had a waddling gait.

Results::

a and b - shows Muscle MRI T2 sequences shows fatty infiltration with atrophy of Glutei (blue arrow) and Quadriceps (Green arrow).
Investigations showed normal creatine kinase levels. Muscle MRI showed fatty infiltration of Glutei and quadriceps (Figure 1). Muscle biopsy was suggestive of CFTD (Figure 2). Clinical exome sequencing revealed homozygous mutations in exon one of ORAI-1 gene in chromosome 12 with two variants - pathogenic variant c.208G>T and variant of uncertain significance c.262C>G.

**Conclusions:** Unique features include slowly progressive myopathy, ophthalmoparesis, absence of immunodeficiency, ORAI-1 mutation with histological CFTD morphology, which has not been reported previously.
OCULO-PHARYNGEAL MUSCULAR DYSTROPHY: PHENOTYPIC AND GENOTYPIC STUDIES IN ABRUZZO

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Background and Aims:: Oculo-pharyngeal muscular dystrophy (OPMD) is a late-onset, inherited muscle disorder, characterized by progressive ptosis, dysphagia and variable proximal limb weakness. The highest prevalence is reported in French Canadians (1:1000)(1) and Bukhara Jews (1:600)(2). Few Italian cases have also been reported(3,4). OPMD is caused by short (GCN)¹¹-¹⁷ expansions in the polyadenylate-binding protein nuclear 1 gene (PABPN1)(5).

Methods:: We summarized the neurophysiological and genetic findings of 15 OPMD patients born in Abruzzo, belonging to 9 unrelated families.

Results:: In our cohort, age at onset was between 42 and 74 years (mean 57). The M/F ratio was 1.14:1. Family history was positive in 13 patients. As expected, ptosis was the most common initial complaint. There was a 6.3-year mean delay before the onset of a second symptom, which was dysphagia in 86.7% of cases. External ophthalmoplegia was present in 73.3% of patients. Two siblings presented cognitive impairment. Genetically, we identified three genotypes, including two GCN¹¹ homozygous patients. Mean age at first evaluation was 68.6 and mean age at genetic screening was 71.5. Creatine kinase levels were mildly elevated in 6 patients. Electromyography, performed in 6 patients, showed myopathic features in three cases. Five patients had ptosis surgery and one patient reported cricopharyngeal myotomy.

Conclusions:: According to our results, OPMD has an estimated minimal prevalence of 1.14 per 100.000 persons in Abruzzo (Figure). A disease cluster can be hypothesized in Caramanico, where OPMD prevalence is about 0.37%. Despite rapid diagnosis through PABPN1 gene screening, OPMD is yet under-recognized and confirmed after several years from symptoms.
onset.
VALIDATION OF THE ITALIAN VERSION OF THE MYASTHENIA GRAVIS IMPAIRMENT INDEX (MGII)

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Background and Aims:: Myasthenia Gravis Impairment Index (MGII) is a recent promising measure developed for MG patients evaluation. It includes a clinical severity evaluation and a patient reported questionnaire. It has been developed in English and has demonstrated feasibility, reliability, and construct validity. Recently its Dutch translation has been validated. The aim of this study is to validate the Italian version of MGII.

Methods:: A multi-step forwards process was used to translate MGII to Italian. We assessed correlations with the following scores: Istituto Nazionale Carlo Besta score for Myasthenia Gravis (INCB-MG), the MG Activities of Daily Living (MG-ADL), the Myasthenia Gravis Composite (MGC), the quality of life 15 for Myasthenia Gravis (QOL15-MG) and the Myasthenia Gravis disability (MG-DIS). We also assessed differences in MGII scores by disease severity with ANOVA Kruskal Wallis test.

Results:: 141 patients were enrolled. The mean MGII total score was 13.3 ± 11.9 (range 0-49), with mean ocular subscore of 3.7 ± 4.7 and mean MGII generalized subscore of 9.6 ± 9.0. As expected, the MGII had a good correlation with the other severity scores. The MGII had lower floor effect (3.5%) than the other measures. 25 patients were assessed in follow-up: as expected, the MGII change scores had moderate correlations with change in other MG severity measures, and lower correlations with quality of life measures.

Conclusions:: The MGII score was cross-culturally validated in a Italian cohort of MG patients. We confirmed its lower floor effect and the correlations with other MG measures including INCB-MG that was not evaluated in previous studies.
ASYMMETRICAL SCAPULAR WINGING, BILATERAL FACIAL MUSCLE INVOLVEMENT AND DISTAL MYOPATHY WITH NORMAL CPK; UNUSUAL FEATURES IN ANTI JO-I POSITIVE POLYMYOSITIS

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Background and Aims: Introduction Polymyositis is an idiopathic inflammatory myopathy which present with typical symmetrical proximal muscle weakness with the evidence of muscle inflammation. The acute inflammation of muscle results in high levels of CPK and has a relapsing remitting course with a good response to anti-inflammatory treatment. We present here a patient presented with a chronic myopathy with relapsing remitting fashion, with asymmetrical scapula winging, and bilateral facial weakness, with predominant distal muscle weakness which was supported by EMG.

Methods: Case report 65 year old woman has presented with 6 year history of progressive muscle weakness. Her initial symptoms were associated with involvement of lower limb proximal muscles and then she noticed difficulty in walking mainly due to slapping of her feet on the ground. There were episodes of worsening of weakness which was responsive to IV methyl prednisolone. She never experienced muscle pains, muscle cramps or positive or negative sensory symptoms.

Results: On examination, She had bilateral foot drop with limb girdle weakness. Additionally, She asymmetrical scapula winging( R>L ) and bilateral facial muscle weakness. Her CPK was found to be mildly elevated.(300).EMG was in favour of myopathy( distal>Proximal ) and her nerve conduction was normal. Muscle biopsy was suggestive of inflammation. Specific antibody testing with Jo-1 results was found to be positive. Figure : A-bilateral facial muscle wasting. B-Asymmetrical scapular winging (R>L).
Conclusions:: Long standing idiopathic inflammatory myopathy can be a diagnostic challenge when presented with atypical features. High degree of suspicion is need as these are treatable conditions with good response to immunosuppressive therapy.
A CASE OF RECURRENT THYMOMA WITH DOUBLE PARANEOPlastic SYNDromes: ARE ANTIBODIES BETTER THAN CLINICAL JUDGEMENT IN PREDICTING THYMOMA RELAPSE?

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Seth GSMC and KEM hospital Mumbai, Neurology, Mumbai, India

Background and Aims:: The co-existence of paraneoplastic CASPR2-antibody mediated Morvan Syndrome(MoS) and myasthenia gravis(MG) with thymoma is extremely rare. We report the case of an elderly male with an autoimmune thymoma-associated MG, whose myasthenic symptoms relapsed after eight years of thymectomy with the co-occurrence of MoS.

Methods:: A 46-year-old farmer with past-history of anti-Acetylcholine Receptor Antibody(AchR-Ab) positive MG (thymoma excision eight years back), came with a two-year progressive history of cramps, occasional involuntary rippling movements over both his thighs, burning paresthesias in distal lower limbs and hyperhidrosis along-with recurrence of Myasthenic symptoms. His detailed workup was done considering provisional diagnosis of peripheral nerve hyperexcitability syndrome and MG with recurrence of thymoma.

Results:: On examination he had myokymia, acral hyperalgesia, fatigable ptosis, and limb-girdle weakness. His slow RNS showed decremental response and EMG showed neuromyotonic discharges with normal motor units. His anti-AchR-Ab, anti-CASPR-2 and anti-Titin antibodies were positive. Fusion FDG-PET and contrast-enhanced CT-Thorax revealed multiple pleural based lesions.A subsequent biopsy of the lesions revealed WHO histology grade-B1 and Masaoka Stage-4 thymomas.He is in complete pharmacological remission for MG and MoS symptoms after eight cycles of cisplatin and paclitaxel-based chemotherapy, gabapentin, and carbamazepine.

Conclusions:: We highlight the rarity of the co-occurrence of MoS, MG and Thymoma. Our clinical suspicion unravelled the relapse of Myasthenia and MoS in our case while evaluating for the cramps and rippling. It is the first description of anti-Titin antibodies in Thymoma-associated MoS to the best of our knowledge, but its significance will need more research.
ACHR MYASTHENIA GRAVIS (MG) ATYPICAL PRESENTATION IN HUMAN IMMUNODEFICIENCY VIRUS (HIV) POSITIVE PATIENT

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Background and Aims:: MG is an autoimmune disease characterized by muscle weakness and fatigability and it is associated with autoantibodies direct to specific muscular proteins like acetylcholine receptor (AchR). The co-occurrence of HIV infection and immune-mediated disorders is known but HIV-MG association is rare.

Methods:: A 30-year-old man without previous medical history, suddenly developed weakness and paresthesias of right limbs, dizziness, postural instability, and intermittent diplopia. Routine blood chemistry, brain MRI, MEPs and SEPs were normal. NCS and electromyography exams showed normal results. CSF analysis revealed 8 cells and mild proteins increase. High serum HIV viral load and CD4+ count 331/mmc were found. HIV specific treatment was started. During hospitalization diplopia and muscular weakness became prominent; moreover, bilateral palpebral ptosis and hypophonia arise. All these symptoms worsened during prolonged exercise. 3-Hz repetitive stimulation to bilateral deltoid and nasalis muscles showed a significant decremental response. Serum antibody against AChR was present (0.52 nmol/l) and CT chest showed thymic hyperplasia. The patient started oral pyridostigmine treatment (120 mg daily) resulting in resolution of hypophonia, muscular weakness but there was incomplete improvement of ptosis and diplopia.

Results:: Few case reports of MG-HIV co-occurrence are reported, but several evidences suggest that causative correlation is probable. Furthermore, previous studies highlight that HIV infection could play a role in the manifestation and natural history of MG.

Conclusions:: MG should always be concerned in diagnostic process of diplopia, even if atypical symptoms are prominent. Despite MG-HIV co-infection is rare, HIV screening test for novel MG diagnosis could be considered.
BARTTER SYNDROME PRESENTING AS PERIODIC LIMB PARALYSIS

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Background and Aims:: Bartter syndrome is a rare autosomal recessive disorder with a defect in the thick ascending limb of the loop of Henle. The estimated prevalence is one in a million. We report a case of Batter syndrome presenting with periodic paralysis.

Methods:: A 15-year-old boy presented with recurrent episodes of sudden onset paralysis of lower and upper limbs mostly nocturnally and after exertion. Each episode lasts 6-10 hours with spontaneous recovery. This continued to happen for the past 8 years. Treatment with Acetazolamide considering hypokalemic periodic paralysis failed. Initially he had 3-4 episodes/year and then 2-3 episodes/month leading to limitation of daily activities and school performance. During episodes, all limbs were flaccid and areflexic. Rest of the exam including blood pressure was normal between episodes. Investigations revealed hypokalemia, metabolic alkalosis and hypercalciuria. A diagnosis of Batter syndrome was made. Spironolactone and oral KCL was started with significant clinical improvement.

Results:: In 1962, Bartter et al. described a clinical syndrome characterized by hypokalemic alkalosis, hyperreninemia, hyperaldosteronism, hypomagnesemia, hypercalciuria and normal blood pressure. It occurs mostly in childhood or adolescence. Cause is yet unknown. Fatigue, proximal muscle weakness and tetany are clinical features. Treatment is with potassium and magnesium repletion, propranolol, spironolactone and prostaglandin inhibitors. Recurrent hypokalemia and chronic renal failure are complications.

Conclusions:: Hypokalemic periodic paralysis should be thoroughly evaluated to unmask any underlying etiology as therapeutic options vary. A proper evaluation would unravel this rare cause of periodic paralysis, which if appropriately treated has an excellent prognosis and in turn will prevent renal failure.
AN AMBISPECTIVE COHORT STUDY OF INFLAMMATORY MYOPATHIES TO UNDERSTAND THE CLINICAL PROFILE AND TEMPORAL TRENDS IN MANAGEMENT

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Background and Aims:: BACKGROUND •Inflammatory myopathies are rare disorders involving multiple systems mainly involving muscles. Their rarity and variable phenotype, there are no standardized protocols for management AIM- To document the clinical profile, treatment response, and regimes used in patients with idiopathic inflammatory myopathies

Methods:: 1.Type of study: A single-center-ambispective cohort observational study 2.Study population: •Patients admitted with a diagnosis of inflammatory myopathy in the department of neurology between 2014 and July 2019 were assessed retrospectively and between November 2019 to March 2021 with a diagnosis of inflammatory myopathy in the department of Neurology were assessed prospectively. •Study protocol- Baseline demographic profile, patient's clinical features, type of inflammatory myopathy, investigations reports including biopsy reports, treatment received, treatment pattern, number of relapses, drugs used, duration of drugs, and the outcomes were assessed. Prospectively patients were assessed for clinical profile, laboratory features, myositis antibody profile, electromyographic findings, treatment received, response to treatment, relapses and chest imaging and PET CT was analyzed

Results:: We analyzed a total of 75 patients of which 62 were retrospective and 14 were prospective cases of which 54 (82%) were dermatomyositis 16 (21%) were polymyositis and 5 (7%) patients were inclusion body myositis. Of these 34 (45.3) were males and 41 (55.6) were females. 19 (25%) of these had relapsed during follow-up. 7 patients refractory to treatment received rituximab and 5 patients received cyclophosphamide.

Conclusions:: Management of IIM varies throughout the world. Our study throws light upon various evidence-based treatment strategies used in the management of IIM which helps in further designing natural history and management studies in the future.
CARDIAC MRI FINDINGS IN DUCHENNE AND BECKER MUSCULAR DYSTROPHY

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Background and Aims:: We sought to determine the prevalence of cardiac involvement in Duchenne and Becker Muscular Dystrophy(DMD/BMD) using MRI and its association with clinical and laboratory parameters.

Methods:: A prospective, observational study was conducted on 24 patients(19 DMD and 5 BMD), genetically confirmed to have DMD/BMD and underwent cardiac MRI on 1.5T Philips Ingenia MRI system.

Results:: In our Dystrophinopathy cohort, mean age=13.46 ± 4.84 years [DMD=11.84 ± 3.2; BMD=19.6 ± 5.37], mean duration=8.08 ± 3.88 years. All had proximal muscle weakness, 70.83% were ambulant and 29.17%-wheel chair bound. 80.95% had variable deletion of exons in DMD gene (82.35% confined to regions between exons 45 to 54), 19.05% had non-sense mutations. Cardiac MRI revealed late gadolinium enhancement(LGE) confined to the left ventricle(LV) consistent with fibrosis in 54.17% of cases[DMD=52.63%; BMD=60%]. In patients with LGE, 53.85%(7 of 13) had reduced LV Ejection Fraction and one patient showed LV dilation. Patients with myocardial fibrosis had longer disease duration(mean duration 9.77 ± 4.38 v/s 6.09 ± 1.87 years, P value=0.017). LGE was not associated with age, genotype, severity of muscle weakness or creatine kinase levels. LGE most often involved the inferolateral mid myocardium and extended to involve other areas with more severe disease.

Conclusions:: There is a high prevalence of subclinical cardiac involvement in DMD/BMD patients which can be detected using Cardiac MRI, that helps in initiating early cardioprotective therapy in this subgroup. Although, our study population is small, there was a small but significant relationship between the development of subclinical myocardial fibrosis and duration of disease.
Background and Aims: Thymolipomas are rare, benign thymic lesions (2%-9% of thymic tumors) and has scarce local and systemic manifestations. Myasthenia gravis (MG)'s association with thymolipomas is uncommon, with just 34 cases reported in the literature until August 2020.

Methods: We report 3 new cases of this uncommon association through a retrospective study at a single institution which were resected between 1992 and 2020.

Results: Three patients initially presented with MG (2 patients were men, and one was a woman) with a median age of 43 years. One patient had positive antiacetylcholine receptor antibodies. All patients underwent a resection of the thymus, even though imaging techniques did not reveal a tumor in 2 cases and showed a thymus nodule in one patient and the histologic study revealed thymolipoma in all three cases. The phenotype was severe in two patients: one patient died after thymectomy due to respiratory distress and the other one has suffered several myasthenic crisis requiring intubation and relapses post thymectomy in spite of well conducted oral medication based on mestinon and corticosteroids. The third one was well controlled after thymectomy.

Conclusions: The possibility of thymolipoma as an anterior mediastinal mass should be kept in mind when dealing with an older age group of myasthenia gravis patients. However, further comparative studies are needed for a more reliable conclusion of the postoperative myasthenia gravis response after resection.
HEREDITARY TRANSTHYRETIN AMYLOIDOSIS WITH POLYNEUROPATHY IN THE NEUROLOGIC CLINIC: RESULTS FROM 12 MONTHS OF GENETIC SCREENING IN THE WESTERN SICILY

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Background and Aims:: Background and aims. Hereditary transthyretin amyloidosis with polyneuropathy (ATTR-PN) is caused by mutations in the TTR gene, leading to misfolded monomers which aggregate generating amyloid fibrils. The clinical phenotype in non-endemic areas is characterized by a late onset with a multisystemic disease affecting the sensorimotor, autonomic functions along with other organs. Hence, the diagnosis may be quite difficult with a relevant misdiagnosis and high costs for the community. We aim to study “red flags” for ATTR-PN to improve recognition and early diagnosis.

Methods:: Methods. A genetic screening was proposed in patients presenting with a sensory-motor idiopathic polyneuropathy and one or more of the following: family history of polyneuropathy or cardiopathy; bilateral carpal tunnel syndrome, cardiac insufficiency, renal amyloidosis, lumbar tract stenosis, autonomic dysfunction, gastrointestinal idiopathic disease, amyloid deposits on biopsy, vitreous opacities, diagnosis of CIDP-not-responsive to standard treatments. Non-parametric analysis has been carried out to underline differences among screened-positive versus negative patients.

Results:: Results. 136 patients underwent genetic testing for suspected for TTR-PN. 25 patients resulted positive (18%). Not significant differences appeared between patients screening positive vs negative depending on age and gender. Patients with a positive genetic test presented a higher frequency of family history of polyneuropathy and cardiopathy, or ATTR (p<0.001) and a reduced frequency of autoimmunity (p=0.013), CIDP (p=0.008).
Conclusions: Conclusions. A systematic screening for ATTR-PN might lead to an increased recognition of the disease even, leading to an earlier diagnosis, identification of asymptomatic carriers, who will be promptly treated after a strict follow-up at the clinical onset.
Background and Aims:: Acute motor axonal neuropathy (AMAN) is a pure motor axonal subtype of Guillain-Barré syndrome presenting with rapidly progressive ascending symmetrical neuromuscular paralysis. Its immunopathogenesis is attributed to autoantibodies that bind to GM1 or GD1a gangliosides often following Campylobacter jejuni infection. We present an unusual case of AMAN where the patient was initially diagnosed with cerebro-vascular event due to acute right-sided hemiparesis and paraesthesia.

Methods:: A 60-year old with a history of hypertension presented with acute right-sided upper and lower limb numbness which in few hours progressed to hemiparesis. Urgent imaging of the brain and cervical spine was performed with no pathological findings. Over the next 24-hours there was rapid progression of the weakness to the contralateral side and respiratory difficulties leading to ventilatory support. This raised suspicion of Guillain-Barré syndrome and a lumbar puncture was performed. The protein level was normal thus not supporting acute inflammatory demyelinating disease. Electrophysiological studies revealed evidence of severe motor demyelinating polyneuropathy with axonal loss and conduction block. The sensory response showed reduced amplitude but normal conduction velocity. Serum samples revealed raised concentrations of IgG antibodies against GM1 and GD1a. These findings led to the diagnosis of AMAN.

Results:: The patient was started on intravenous immunoglobulin treatment. She has received four cycles but with slow recovery. She is now off the ventilator with spontaneous breathing but still unable to mobilise.

Conclusions:: The diagnosis was challenging due to the unusual clinical presentation where the patient had also sensory symptoms and the motor deficit was asymmetric and descending in nature.
AN ATYPICAL CASE OF DERMATOMYOSITIS ASSOCIATED WITH CLEAR CELL RENAL CELL CARCINOMA

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Background and Aims:: Up to 30% of idiopathic inflammatory myopathies cases are associated with an underlying malignancy. Renal tumours have only rarely been described in patients with DM and, to the best of our knowledge, this is the second report of clear cell renal cell cancer (RCC) presenting with dermatomyositis.

Methods:: We describe a 43-year male, without any previous comorbidities, who presented with acute onset and progressive quadriparesis of two weeks duration. After initial routine hemogram and biochemical evaluation, appropriate imaging followed tissue biopsy clinched the diagnosis.

Results:: On initial evaluation patient had power MRC grade 2/5 in bilateral proximal upper limbs and lower limbs and 4/5 in distal limbs, with a maculopapular rash on upper chest and back. At presentation, CK (creatine kinase) was 22,000 U/L (N=39-308). Muscle biopsy showed mild endomysial inflammatory infiltration comprising of T helper and suppressor cells and positive for Mi2a, Ku, Jo-1, Ro-52. Whole body PET was done which revealed uptake in the right kidney. Suspecting paraneoplastic Dermatomyositis, he was started on pulse methylprednisolone followed by oral steroids. Subsequently his power improved, and the rash disappeared completely. After 6 weeks, elective partial nephrectomy was done, and histopathology showed clear cell RCC (WHO ISUP Grade I). At 4 weeks follow up, power bilateral upper and lower limbs was 5/5, CK reduced to 237U/L and patient was on tapering of oral steroids and Mycophenolate 500mg BD.
Conclusions: Though rare, RCC can lead to dermatomyositis and instead of considering it as an incidentaloma, early tumour removal leads to better outcomes.
PATISIRAN IN PATIENTS WITH HATTR AMYLOIDOSIS POST-ORTHOPEDIC LIVER TRANSPLANT: 12-MONTH RESULTS

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Background and Aims:: Hereditary transthyretin-mediated (hATTR) amyloidosis is a progressive, debilitating disease. Orthotopic liver transplant (OLT) eliminates variant transthyretin (TTR) to slow progression in early-stage hATTR amyloidosis. Patisiran reduces production of variant and wild-type TTR, as shown in patients who had not undergone OLT in the APOLLO study.

Methods:: Phase 3b open-label study (NCT03862807) to evaluate safety, efficacy, and pharmacokinetics (PK) of patisiran in patients with hATTR amyloidosis with polyneuropathy and disease progression post-OLT. Patients received patisiran 0.3 mg/kg intravenously q3w for 12 months.

Results:: Twenty-three patients enrolled; median age 58.0 years, 13 (56.5%) male, and 15 (65.2%) had V30M mutation. At baseline, 1 (4.3%) patient had polyneuropathy disability (PND) score I, 9 (39.1%) PND II, and 13 (56.5%) PND IIIA/B. Five patients (21.7%) had New York Heart Association (NYHA) classification I, 5 (21.7%) NYHA II, and none had NYHA III/IV at study baseline. At month 6, the mean (SEM) TTR level was 21.2 (3.7) mg/L, representing an 89.2% reduction from baseline. All patients experienced ≥1 adverse event (AE) and 5 patients experienced at least one serious AE; majority of AEs were mild or moderate in severity. Liver function tests were stable in the majority of patients. One patient experienced transplant rejection deemed unrelated to patisiran.

Conclusions:: To date, reduction in serum TTR levels and safety profile of patisiran in patients with hATTR amyloidosis with polyneuropathy with disease progression post-OLT has been consistent with results from APOLLO. Patisiran has the potential to address an unmet need in these patients.
Background and Aims:: Allgrove syndrome is a rare, autosomal recessively inherited syndrome characterised by achalasia, alacrima, adrenal insufficiency and progressive neurological dysfunction. Afflicted individuals usually manifest with 2-4 of these symptoms and most cases have no positive family history. Mutations in ALADIN gene located on chromosome 12q13 are responsible.

Methods:: A 46-years old gentleman, born of non-consanguineous marriage, presented with progressively increasing proximal lower and upper limb weakness for past 20 years. He had concomitant dysphagia and nasal intonation complicated by recurrent dyspepsia for past 5 years, whose evaluation lead to a diagnosis of achalasia. He developed complaints of severe dryness of eyes since 5 years and has been on lubricating eyedrops. He developed erectile dysfunction since past 3 years, whose evaluation lead to a diagnosis of concomitant azoosperma. Examination revealed a postural hypotension with wasting of small muscles of hand and tongue, with fasciculations. Power in the proximal and distal joints was MRC grade 4/5 and 5/5 respectively. Spasticity was present, reflexes were brisk and plantars were extensor.

Results:: Nerve conduction studies revealed an axonal neuropathy with electromyography suggestive of preganglionic neurogenic involvement. Autonomic function tests revealed severe sympathetic-parasympathetic involvement. MRI brain and spine were normal. Next generation clinical exome sequencing revealed a homozygous c.C43A/p.Gln15Lys missense mutation on exon 1 of the ALADIN gene on Chromosome 12.

Conclusions:: Allgrove syndrome should be suspected in patients presenting with features of CNS/PNS dysfunction with achalasia, alacrima and/or adrenal insufficiency. Although, no treatment modalities exist, earlier diagnosis can lead to proper counselling, symptomatic management and incorporation in research trials, which can hopefully provide a cure in the future.
EVALUATION OF COMORBIDITIES IN MYASTHENIA GRAVIS: THE EXPERIENCE OF AN ITALIAN CENTER

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Background and Aims:: Myasthenia gravis (MG) is an autoimmune disorder of neuromuscular junction; management of therapy in MG can be very complex, because of the most common used drugs can worse chronic comorbidities and increase disabilities and assistance need. We evaluated the prevalence of comorbidities among a cohort of MG patients and a control group.

Methods:: Patients with diagnosis of MG where collected from the Italian centre of Palermo. Control patients were collected with a web-available questioner asking after age and sex, questions about chronic diseases. Prevalence of main chronic disorders found in MG patients was compared with control cases using chi squared test.

Results:: 125 MG Patient (65 M) were analysed and compared with 200 unaffected controls. A significative difference (P<0.05) was found comparing results for hypertension, hypercholesterolemia, diabetes, cardiovascular disorders, osteoporosis.

Conclusions:: Our findings show that a lot of comorbidities are more common than in general population in MG patients. Hence the diagnosis and therapy of MG can be very difficult because of comorbidity can mimics symptoms and can be worsened by administration of steroid and immunosuppressors agents routinely used in MG. MG type and comorbidities risk should be carefully considered for a positive outcome.
CONGENITAL MYASTHENIC SYNDROMES: PHENOTYPIC VARIABILITY AND THE DIAGNOSTIC CHALLENGE

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Background and Aims:: Congenital myasthenic syndromes (CMS) are a rare and heterogeneous group of neuromuscular junction disorders, caused by genetic mutations. It has an estimated incidence of 9.2 cases per million in children under 18 years-old. Dok-7 deficiency (OMIM#254300) accounts for less than 10% of all CMS cases. The purpose of this report is to emphasize the importance of genetic testing to complete a complex diagnosis of CMS, whose phenotype initially suggested congenital myopathy.

Methods:: This article was written based on data of medical record of a 23 months-old, female patient, diagnosed with CMS caused by Dok-7 deficiency.

Results:: Female, 23 months-old, daughter of a consanguineous couple, had a history of weak crying, left eyelid ptosis and global hypotonia observed at birth. Developed weight and height deficit and motor delay, in addition to dysphagia for fluids and frequent hospitalizations for pneumonia. On physical examination, she presented scaphocephaly, asymmetric bipalpebral ptosis, ogival palate, retrognathia, ears rotated posteriorly, ramp shoulders, kyphoscoliosis, global hypotonia, predominantly axial, involving mainly the neck musculature, hyperreflexia and exhaustible clonus in the feet. Electroneuromyography, using a low frequency repetitive stimulation technique, showed an electrodecrement of up to 50%, showing postsynaptic junction disorder. The genetic panel revealed a mutation in the heterozygous DOK7 and CHRNA1 gene, with pathogenic significance, confirming CMS.

Conclusions:: CMS may mimic many classic manifestations of myasthenia, but they can also present wide phenotypic variability, as in this case. Due to its rarity the diagnosis of CMS is a challenge, but the suspicion must be raised when we encounter early onset hypotonia.
Background and Aims:: Myasthenia gravis (MG) is an autoimmune disease characterized by muscle weakness. It is associated with antibodies to neuromuscular junction proteins such as AChR and MuSK. In mothers with AChR-MG transplacental passage of antibodies to foetus may cause neonatal MG. We report a case in which the same patient suffered from MG twice in her life.

Methods:: A 18-year-old female patient was referred to our Institution for ptosis, diplopia and mild generalized muscle weakness. After a single fiber EMG and a positive AChR antibody assay, MG was diagnosed and patient underwent to thymectomy with histological findings of hyperplasia. Pyridostigmine treatment led to minimal manifestations according to Myasthenia gravis foundation of America classification. At a later time we knew that patient’s mother was also affected by AChR-MG from the age of 27 and our patient suffered from neonatal MG (difficulty with latching on, breastfeeding and crying) in postpartum period: a course of liquid pyridostigmine was beneficial and after a month neonatal MG signs were definitely absent.

Results:: As maternal IgGs disappear after 6 months, a delayed action of mother’s AChR autoantibodies can be excluded. Actually in this case, the same autoimmune disease developed after many years.

Conclusions:: To our knowledge this is the first case of two different manifestation of MG in the same patient and it may be helpful to understand how environment and genetic play a crucial role in autoimmune disease.
Background and Aims:: Background and aims. Hereditary transthyretin amyloidosis with polyneuropathy (ATTR-PN) is caused by mutations in the TTR gene, leading to misfolded monomers which aggregate generating amyloid fibrils. The clinical phenotype is heterogeneous, characterized by a multisystemic disease affecting the sensorimotor, autonomic functions along with other organs.

Methods:: Methods. All patients were assessed with a standardized questionnaire on well-recognized symptoms of ATTR-PN, neurophysiological evaluation (ENG/EMG) and bioimpedance analysis. The data are presented as means and standard deviations. Pearson’s correlation has been carried out when appropriate. A linear regression model has been created to identify associated variables to pathology severity.

Results:: Results. 16 patients with ATTR-PN (62.8±8.9 years; 165.0±12.5 cm; 74.9±14.9 kg) of which 7 women have been recruited. The data indicate that at increased pathology severity as indicated by FAP, increased presence of bilateral carpal tunnel syndrome and increased overall symptoms of neuropathy (Table 1). A concomitant decrease of the CMAP amplitude of the median nerve was also observed (Table 2). FAP degree alone may explain 45% of the decrease of the median nerve amplitude. Also, when severity of disease is associated to bioimpedance analysis (BIA) we observe increased presence of weight loss with increased severity, which is associated to a reduction only in lean muscle mass. Increased FAP is also strongly associated to a reduction of the phase angle.
**Table 1. Descriptive measures of bioimpedance analysis**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean±st.dv</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFM (kg)</td>
<td>52.2±11.0</td>
</tr>
<tr>
<td>FM (kg)</td>
<td>22.6±7.12</td>
</tr>
<tr>
<td>BCM (kg)</td>
<td>24.8±7.99</td>
</tr>
<tr>
<td>PA (°)</td>
<td>4.94±1.33</td>
</tr>
</tbody>
</table>

**Table 2. Descriptive measures of ENG of the median nerve**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean±st.dv</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal motor latency (ms)</td>
<td>3.74±1.45</td>
</tr>
<tr>
<td>Amplitude (mV)</td>
<td>8.50±6.17</td>
</tr>
<tr>
<td>Velocity (m/s)</td>
<td>55.5±3.00</td>
</tr>
</tbody>
</table>

**Correlation Matrix**

<table>
<thead>
<tr>
<th>Correlations</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAP vs Bilateral presence of carpal tunnel syndrome</td>
<td>0.731</td>
<td>0.0001</td>
</tr>
<tr>
<td>FAP vs Neuropathy symptoms</td>
<td>0.583</td>
<td>0.014</td>
</tr>
<tr>
<td>FAP vs Lumbar stenosis</td>
<td>0.52</td>
<td>0.040</td>
</tr>
<tr>
<td>FAP vs Weight loss</td>
<td>0.663</td>
<td>0.004</td>
</tr>
<tr>
<td>FAP vs Median Nerve Amplitude</td>
<td>-0.674</td>
<td>0.016</td>
</tr>
<tr>
<td>FAP vs PA</td>
<td>-0.703</td>
<td>0.002</td>
</tr>
<tr>
<td>Weight loss vs BCM</td>
<td>-0.550</td>
<td>0.027</td>
</tr>
</tbody>
</table>

**Linear Regression**

FAP vs Median Nerve Amplitude $R^2 0.455$, $p<0.001$

**Conclusions:** Conclusions. The progression of bilateral carpal tunnel syndrome, polyneuropathy, lumbar stenosis and weight loss is related to the FAP grade in ATTR-PN. Also, we propose BIA as an important tool for disease progression in ATTR-PN.
MISDIAGNOSIS OF CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (CIDP): A TWO YEARS FOLLOW-UP STUDY.

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Background and Aims:: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an immune-mediated disorder involving peripheral nerves, characterized by sensory alteration and weakness with gradual progression over years leading to disability. Diagnosis is obtained through clinical history, neurological examination, serum and liquoral biomarkers and neurophysiology. Neurophysiological criteria proposed by European Federation of Neurological Societies and Peripheral Nerve Society (EFNS/PNS) are used for the diagnosis allowing high sensitivity and specificity. However, several conditions can mimic CIDP.

Methods:: In this study we observed 53 patients with diagnosis of CIDP according to EFNS/PNS criteria, followed in an ambulatory setting for two years. After two years of follow-up a revision of EFNS/PNS criteria was performed again through a neurological evaluation, serum and neurophysiologic assessment.

Results::

53 patients have been enrolled, satisfying EFNS/PNS criteria at study start. Clinically 34 (64%) patients with typical CIDP, 13 (24%) with not defined CIDP and 19 (12%) with atypical CIDP, including 2 (4%) with distal acquired demyelinating symmetric neuropathy (DADS), 1 (2%) with purely motor, 3 (6%) with Lewis-Sumner syndrome (LSS). However, after two-years of follow-up in 18 patients EFNS/PNS criteria were any more satisfied leading to a different diagnosis: 7 (13%) diabetes mellitus, 5 (9%) monoclonal gammopathy of undetermined significance (MGUS), 1 (2%) hereditary amyloidosis ATTR, 1 (2%) anti-myelin-associated glycoprotein (anti-MAG) and 4 (8%) deficit of vitamin B12.

Conclusions:: Our study showed that other diagnosis can mimic CIDP at clinical onset; a careful revision of criteria is needed during the follow-up to achieve the correct diagnosis and choose the better treatment option for patients with neuropathies.
OUTCOME MEASURES CHARACTERIZATION IN AN ITALIAN COHORT FOR CMT PATIENTS STRATIFICATION

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Background and Aims:: Charcot-Marie-Tooth (CMT) disease is the most common inherited neuromuscular disorder, with variable age of onset (from infancy to adulthood) and a broad phenotypic spectrum. Several motor function and disability scales in CMT patients are available. The aim of this study is to better characterize CMT in its forms, also providing a clinical follow-up tool.

Methods:: We selected a cohort of 40 patients with confirmed diagnosis of CMT. For each patient we collected natural history, genetic characterization and electrophysiological data. All patients underwent clinical evaluation including following assessments: Muscle strength evaluated by Medical Research Council score, CMT Neuropathy Score (CMTNS) second version and CMT Functional Outcome Measure (CMT-FOM) scale.

Results:: We have recruited 40 CMT patients, 23 women and 17 males, aged between 23 and 65 years at the time of evaluation. In our cohort the most frequent form was CMT1A (29 patients) followed by hereditary Neuropathy With Liability to Pressure Palsies (HNPP) (N=7), CMT2A (4 patients) and CMT2N (1 patient). For each patient we collected and analyzed clinical data correlating them to the disease genotype, highlighting different degrees of disability and motor impairment in each group.

Conclusions:: The use of the two scales allows a more specific characterization of the different form of CMT, defining any specifics or limits, useful not only in clinical practice but also as outcome measures reference for potential future clinical trials.
QUADRIPARESIS SECONDARY TO CEREBRAL VENOUS SINUS THROMBOSIS: RARE CAUSE OF ACUTE FLACCID WEAKNESS

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Background and Aims: Cerebral venous sinus thrombosis (CVST) presents with headache, seizures, focal deficits, altered consciousness and papilledema. False localising sign in the form of sixth cranial nerve palsy is commonly seen. Other cranial nerve palsies reported in CVST are oculomotor, facial, trigeminal and trochlear nerve palsies. Polyradiculopathy if seen, is in the form of reduced deep tendon reflexes (DTR), however dense quadriparesis with trunk and neck involvement and areflexia is rarely seen.

Methods: 16 year-old obese male had flaccid quadriparesis with severe neck and trunk weakness over 10 days followed by headache and blurring of vision. Examination revealed signs of raised intracranial pressure in the form of bilateral grade 4 papilledema, finger counting on right side and no light perception on left side along with bilateral 3rd, 6th, 7th and 5th cranial nerves palsies, power of grade 2/5 with hypotonia and areflexia.

Results: Gadolinium enhanced magnetic resonance imaging (Gd-MRI) revealed thrombosis of right transverse and sigmoid sinuses. Gd-MRI spine was unremarkable. CSF pressure by lumbar puncture was 34 mmHg. He started improving immediately after CSF drainage and acetazolamide. On 2 months follow-up, his mRS was 1. Weakness was likely due to polyradiculopathy secondary to transmitted raised intracranial pressure which was reversible once pressure was reduced.

Conclusions: Acute flaccid weakness due to polyradiculopathy secondary to CVST is another false localising sign along with multiple cranial palsies and denotes completely reversible dysfunction of spinal nerve roots.
WHAT IS THE CLINICAL SIGNIFICANCE OF THE FACIAL-SPARING PHENOTYPE IN FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY? A NATION-WIDE CROSS-SECTIONAL STUDY

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Background and Aims:: Does the FSHD facial-sparing phenotype have peculiar features, regarding degree of severity, risk of disease in relatives and the size of D4Z4 repeat array?
Methods:: A multicenter cross-sectional study included 460 subjects (125 with facial-sparing phenotype and 328 subjects with the complete FSHD phenotype) from the Italian National Registry for FSHD. The phenotypic classification was obtained by applying the Comprehensive Clinical Evaluation Form (CCEF) and the degree of muscle impairment was measured as FSHD score (0-15).
Results:: We found that subjects with facial-sparing phenotype (B1 clinical category) have a significantly milder phenotype in comparison with subjects presenting classic FSHD phenotype (P value <0.001). Out of 33 families having a proband with facial-sparing phenotype in 54.5%, the proband was the only participant expressing a myopathic phenotype. Interestingly, of the 125 clinically assessed B1 subjects, 36% did not carry a D4Z4 allele with 10 or fewer repeat units.
Conclusions:: This study found that the facial-sparing phenotype defines a distinct nosological entity with different disease course and lower penetrance. It is recommended that clinicians use the CCEF for clinical classification and study the extended family to provide the most adequate clinical management and genetic counseling. The same phenotype was found in participants carrying D4Z4 alleles of normal size in contrast to the indication that a positive molecular test is the only determining aspect for FSHD diagnosis.
IMMUNOGLOBULINE THERAPY IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY: INTRAVENOUS VERSUS SUBCUTANEOUS ADMINISTRATION.

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Background and Aims:: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired sensory-motor neuropathy with autoimmune pathogenesis. First line treatments include corticosteroids, plasmapheresis, and immunoglobulin therapy. The classic form of immunoglobulin administration is intravenous, however subcutaneous immunoglobulin (SCIG) therapy became a valid alternative option especially for maintenance therapy. Cross-sectional study to compare long-term response to intravenous immunoglobulin (IVIG) and SCIG.

Methods:: We selected a cohort of patients suffering from CIDP for which we collected data about age and onset symptoms, neurophysiology, comorbidities, clinical course and response to therapy. Patients underwent regular neurological evaluations every 3 months, including Medical Research Council Sum-Score (MRC-SS), Inflammatory Neuropathy Cause and Treatment scale (INCAT), Inflammatory Neuropathy-Rasch-Built Overall Disability Scale (I-RODS), patient treatment preference and treatment satisfaction questionnaire.

Results:: We’ve evaluated 150 patients (65% male) in a range of age of 22-88 years and with an average of 10 years illness duration. 51 patients require regular administration of IG, which 36 are treated with IGIV infusions every 30 or 60 days, while 15 patients have switched to SCIG treatment with a frequency administration of 1, 2 or 3 times a week. Both forms of administration are equally safe and tolerated and allow to stabilize the disease progression. We notice that compliance with the use of SCIG is also greatly affected by the practicality or difficulty in home management nevertheless it is globally preferred.

Conclusions:: Both routes of administration are effective maintenance therapies. Our data confirm those reported in literature and expand the knowledge about the response to immunomodulatory therapy in CIDP.
IMMUNE-MEDIATED RIPPLING MUSCLES WITH MYASTHENIA GRAVIS, THYMOMA, AND OTHER IMMUNE-MEDIATED DISORDERS: A REVIEW OF THE LAST 25 YEARS

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Background and Aims:: In 1996, we described the first case of rippling muscles with myasthenia gravis. This patient also had a thymoma. Since then, numerous cases of rippling muscles with myasthenia gravis have been reported. Some have had thymomas, but other immune-mediated disorders have also been reported. This review will attempt to categorize these patients and their associated disorders.

Methods:: The literature will be reviewed and the published data from the patients described to date summarized. This will include immune-mediated rippling muscles with and without myasthenia gravis.

Results:: The most common immune disorder associated with rippling muscles is myasthenia gravis with over 20 cases reported to date. Thymoma also has been reported in about 20% of the cases. Rippling muscles with myasthenia gravis have also been reported after viral infections, yersinia enterocolitica, bronchial asthma, alopecia areata, and thymitis. There have also been isolated cases reported with autoimmune hemolytic anemia, lymphoma, pernicious anemia, sarcoidosis, breast and prostate cancer, and after taking statins. There have been rare cases of immune-mediated rippling muscles without evidence of myasthenia gravis or positive acetylcholine receptor antibodies.

Conclusions:: Patients who present with rippling muscles and no family history of this should be assumed to have myasthenia gravis plus or minus a thymoma until proven otherwise. Other immune-mediated disorders should also be reported, especially if their onset is temporally related to the rippling muscles.
D4Z4-PATHIES: EVIDENCE FROM THE ITALIAN NATIONAL REGISTRY FOR FSHD

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Background and Aims:: The Italian Clinical Network for FSHD (ICNF) has established the Italian National Registry for FSHD (INRF), collecting data from patients affected by Facioscapulohumeral dystrophy (FSHD) and their relatives from fourteen centers distributed across Italy.

Methods:: Starting from 2007, INRF has gathered data from molecular analysis, clinical evaluation, anamnestic information and family history from more than 4000 participants. INRF includes sociodemographic information and healthcare information such as molecular analyses, anamnestic records and clinical features based on a standardized medical-reported form called CCEF.

Results:: The analysis of the distribution of D4Z4 reduced allele revealed that 15.2% of index cases from INRF carry a very short allele with 1-3 D4Z4 allele, 70.6% carry alleles with 4-8 D4Z4 repeats, 14.1% alleles with 9-10 D4Z4 allele. We observed a more homogenous FSHD phenotype among index cases with 1-3 D4Z4 reduced allele, although a significant percentage of them (21.8%) showed atypical features. Among index cases with larger D4Z4 repeats allele, 56.4% of them displayed a classical FSHD phenotype with facial and scapular muscle weakness, whereas 13% presented incomplete phenotype with facial weakness or scapular girdle involvement. Notably, 24.3% of index cases with 4-10 D4Z4 allele showed more complex phenotypes with atypical clinical features.

Conclusions:: Our research activities highlight that among carriers of D4Z4 reduces alleles and their families it is possible to recognize distinct nosological entities with different disease courses and lower penetrance. We suggest introducing a new term, D4Z4-pathies, to better define the clinical variability of disease.
**Background and Aims:** There is a wide variability of phenotype expression in patients affected with Charcot-Marie-Tooth disease type 1A (CMT1A) but no univocal explanations are available. Single nucleotide polymorphisms (SNPs) could play a role in modulating clinical picture in several conditions but definite evidence regarding CMT1A is missing.

**Methods:** Twenty-three CMT1A patients were enrolled and SNPs rs4280262 in LITAF, rs6875902, rs3763022 and rs230403 in SH3TTC2, rs10910527, rs4649265, rs7536385 and rs1547740 in SIPA1L2, H63D and C282Y in HFE were analyzed. Each patient was clinically assessed by several validated scales in order to quantify sensory and motor involvement.

**Results:** The presence of LITAF rs4280262, SH3TTC2 rs3763022, SIPA1L2 rs10910527, rs4649265 and rs7536385 was associated with a more severe motor phenotype. SH3TTC2 rs2304034, SH3TTC2 rs6875902 and SIPA1L2 rs1547740 did not appear to affect the severity of the phenotype. HFE H63D was associated with a lower strength in foot dorsiflexion (p 0.022). We observed an inverse correlation between the number of SNPs and the meters walked at 6MWT (p 0.011) and a positive relationship between the number of SNPs and the burden of disability in the upper (p 0.012) and lower limbs (p 0.019) and sensory involvement (p 0.025).

**Conclusions:** SNPs could play a role in modulating CMT1A phenotype, in particular H63D in HFE which was not previously described. Our results showed a possible summation effect of the individual SNPs in influencing the phenotypical expression of the disease. Certainly, larger case studies are needed in order to confirm these observations.
Background and Aims:: Myasthenia gravis (MG) is an autoimmune neuromuscular junction disease. An association between thymic epithelial neoplasms and MG is well known. However, it is rarely associated with hematologic malignancies. In particular, very few cases of lymphoblastic lymphoma (LL) involving the thymus and MG have been reported.

Methods:: A case report of a patient with MG and a malignant LL involving the thymus.

Results:: A 45-year-old woman was admitted with a 1 month history of bilateral, asymmetric and fluctuating ptosis. The diagnosis of MG was made on the basis of the clinical data, a positive neostigmine test, elevation of acetylcholine receptor antibodies and EMG with repetitive nerve stimulation tests revealing neuromuscular junctional dysfunction. Chest CT demonstrated a solid mass at the anterior mediastinum that was considered to be a thymoma. Total thymectomy was subsequently performed. The anatomapathological study concluded to T-cell lymphoblastic lymphoma.

Conclusions:: An association between lymphoid malignancies and MG have been reported in the literature. However, coexistence of LL involving thymus and MG are rare. Myasthenic symptoms either preceded, succeeded or were present at the time of diagnosis of lymphoblastic lymphoma which is the case of our patient. Although the causal relationship between lymphoblastic lymphoma and the autoimmune response cannot be demonstrated, it is tempting to speculate that the T-cell defect induced by lymphoma and subsequent chemotherapy might have contributed to the development of autoimmunity.
NEURALGIC AMYOTROPHY AFTER SHINGLES VACCINATION

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Background and Aims:: Neuralgic amyotrophy (aka Parsonage-Turner Syndrome) is often idiopathic but, in about half of the cases, may follow strenuous exercise, pregnancy, surgery, bacterial or viral infections, or vaccinations.

Methods:: Review clinical, laboratory, imaging, and electrophysiological data of a patient who developed neurologic amyotrophy after receiving a vaccination for shingles.

Results:: A 56-year-old woman developed severe pain in the right shoulder and arm 2 weeks after receiving herpes zoster vaccine in the right arm. Within several weeks of the pain, she noted severe weakness of shoulder elevation. The pain improved over the next 2-3 months. Her neurological examination, 2 months after onset of symptoms, was pertinent for severe weakness of the right shoulder abduction, shoulder external rotation and elbow flexion (MRC 4-/5). Elbow extension and hand/wrist strength were normal. There was no sensory loss. The right biceps reflex was absent while the left biceps, and both triceps reflexes were +2. MRI of the cervical spine showed a mild C4-5 disc bulging with no foraminal stenosis at C4-5 or C5-6 on the right. Both motor and sensory nerve conduction studies were normal including median and lateral antebrachial sensory responses. Needle examination showed prominent active denervation with reinnervation in the right supraspinatus, infraspinatus, deltoid and biceps muscles. The brachioradialis, pronator teres, rhomboid and cervical paraspinal muscles were normal.

Conclusions:: This patient developed classical manifestations of neuralgic amyotrophy soon after herpes zoster vaccination in the ipsilateral arm. She had acute pain followed by weakness/denervation in the right suprascapular, axillary and musculocutaneous nerves.
USE OF DRUGS FOR ATTRV AMYLOIDOSIS IN THE REAL WORLD: HOW THERAPY IS CHANGING SURVIVAL IN A NON-ENDEMIC AREA

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Background and Aims:: Background: Over the past decade, 3 new drugs have been approved for the treatment of familial TTR amyloid polyneuropathy; aim of this work is to analyze if current therapies have prolonged survival in patients affected by ATTRv amyloidosis.  
Methods:: The study was conducted retrospectively, analyzing the medical records of 105 patients with genetic diagnosis of familial amyloidotic polyneuropathy followed at the 2 referral centers for the disease in Sicily (University of Messina and Palermo ). Of these, 71 patients received disease-modifying therapies, while 34 received only symptomatic treatments or no therapy  
Results:: The most used treatment in our patient cohort was tafamidis followed by liver transplant, patisiran, inotersen and diflunisal. Survival was significantly longer in treated vs untreated patients. Patients diagnosed in the early stage of the disease (PND 0-1) had a significantly longer survival than those diagnosed in the late stage (PND 2-3-4).  
Conclusions:: As predicted in previous reports, the prevalence of transthyretin amyloidosis is significantly increasing in Sicily Island thanks to a greater attention to this pathology. The disease modifying therapies, up to now in percentage mainly represented by tafamidis, have significantly improved the survival of patients. When patients are diagnosed at PND stage 1, their overall survival is longer.
RELATIONSHIP OF PHARMACOKINETICS AND PHARMACODYNAMICS TO APITEGROMAB EFFICACY IN PATIENTS WITH LATER-ONSET SPINAL MUSCULAR ATROPHY (TYPES 2 AND 3 SMA): RESULTS FROM THE TOPAZ STUDY

Thomas Crawford1, Amy Place2, Doreen Barrett3, Shaun Cote4, George Nomikos5, Guochen Song5, Sanela Bilic6, Ashish Kalra7, Mara Sadanowicz8, Janet O’Neil8, Ryan Iarrobino9, Nathalie Kertesz2, Yung Chyung5


Background and Aims:: Apitegromab is an investigational, fully human, monoclonal antibody that inhibits myostatin activation by specific binding to myostatin proforms, promyostatin and latent myostatin. We will present data, from the Phase 2 TOPAZ clinical trial (NCT03921528), on the relationships of pharmacokinetics (PK) and pharmacodynamic (PD) (marker of target engagement, latent serum myostatin levels) to apitegromab efficacy.

Methods:: The phase 2 study of apitegromab was a 52-week trial conducted in subjects with late-onset SMA (age 2-21 years). Patients received IV apitegromab every 4 weeks, either as monotherapy or as an adjunct to nusinersen. Primary endpoints were efficacy (assessment of motor function improvements via the Hammersmith scale scores) and safety.

Results:: In the TOPAZ study, 58 patients were dosed in 3 cohorts. Cohort 1 enrolled 23 ambulatory patients with SMA. Cohort 2 enrolled 15 patients with nonambulatory Type 3 SMA or Type 2 SMA. Patients in cohorts 1 and 2 received 20 mg/kg apitegromab. Cohort 3 enrolled 20 patients with Type 2 SMA and received either 2 mg/kg or 20 mg/kg in a double-blind, randomized 1:1 manner. Relationship of PK/PD measures with motor function efficacy endpoints of apitegromab will be presented.

Conclusions:: This information is helpful in understanding latent myostatin dynamics, apitegromab’s effects in SMA and to the planning of future studies. Apitegromab has the potential to be the first muscle-directed therapy to address motor function impairment affecting patients with Types 2 and 3 SMA.
NORMATIVE ELECTROPHYSIOLOGIC REFERENCE VALUES FOR THE LATERAL AND MEDIAL ANTEBRACHIAL CUTANEOUS NERVES AMONG ADULT SUDANESE POPULATION

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Background and Aims:: Nerve conduction studies (NCS) help in assessing peripheral nerve injuries by localizing focal lesions, defining severity, and distinguish axonal from demyelinating disorders. Objective: To obtain electrophysiological normative values for the lateral and medial antebrachial cutaneous nerves (LACN and MACN) among healthy adult Sudanese populations.

Methods:: This is a descriptive, analytic, cross-sectional study conducted in El Magzoub Neuroscience Center Khartoum, Sudan. It included 200 LACN and 200 MACN from eligible Sudanese volunteers using standardized techniques.

Results:: The mean ± SD values of the onset and peak latencies (ms), amplitude (µV), and conduction velocity (m/s) of LACN for the whole participants were 1.75 ± 0.31, 2.27 ± 0.31, 22.77 ±11.71 and 71.01 ±14.06 respectively. Parameters of the left LACN were 1.65 ± 0.29, 2.20 ± 0.27, 23.43 ± 13.18 and 75.59 ± 15.27. While that of the right LACN were 1.85± 0.3, 2.34 ± 0.33, 22.11 ± 10.04 and 66.43 ± 11.0 respectively. The findings of the MACN for the whole participants were 1.67 ± 0.33, 2.17 ± 0.43, 15.53 ± 9.01, and 74.69 ± 13.91, respectively. Values of the left MACN were 1.64 ±0.35, 2.14 ± 0.42, 15.47 ± 8.86 and 76.84 ± 14.2, and those of the right LACN were 1.69 ±0.31, 2.20 ±0.44, 15.22 ±9.21 and 73.43±13.47 respectively.

Conclusions:: Proper positioning of electrodes and the use of low-intensity stimulation are essential measures to obtain a satisfactory recording for these nerves. Furthermore, anthropometric measures, particularly gender, sidedness, and temperature must be taken into consideration as they influence the values of the obtained recordings.
IMPACT OF COVID-19 ON A GROUP OF PATIENTS WITH MYASTHENIA GRAVIS

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Background and Aims:: Myasthenia gravis (MG) is an autoimmune disease affecting the neuromuscular junction. The most severe complications are bulbar exacerbations and myasthenic crises, of which respiratory infections represent an important risk factor. The aim of the present study is to evaluate the impact of COVID-19 on MG patients.

Methods:: We retrospectively reviewed clinical records of all SARS-CoV2 positive MG patients who regularly attended the myasthenic outpatient clinic at the Treviso Hospital from March 2020 to March 2021. For each patient, we collected clinical features, MG outcome and COVID-19 severity using a WHO- and SIAARTI-based classification.

Results:: Nineteen patients have been enrolled (10 females, 9 males, mean age 62 years). COVID-19 severity resulted as follows: 1 patient was asymptomatic, 10 had mild symptomatic disease/pneumonia, 6 had severe pneumonia, 1 had moderate-severe acute respiratory distress syndrome (ARDS), 1 died. MG outcome was unchanged in 15 patients, an increase/change of therapy was necessary in 2, there were 1 bulbar exacerbation and 1 myasthenic crisis treated with intravenous immunoglobulins. In 4 patients we found other known exacerbating factors, in particular: infections other than SARS-CoV2 and medications to use with caution in MG.

Conclusions:: This is a preliminary group of MG patients with COVID-19. A high prevalence of severe COVID-19 cases have been found (7/19 had severe respiratory manifestations and 1/10 died). On the other hand, MG outcome does not seem to be associated with COVID-19 severity. Larger studies are necessary to confirm these data and to evaluate associations between COVID-19 severity, MG severity and baseline therapy.
NORMAL NEUROPHYSIOLOGIC PARAMETERS OF THE TIBIAL NERVE AMONG ADULT HEALTHY SUDANESE POPULATION

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Background and Aims:: Nerve conduction studies (NCSs) are noninvasive diagnostic tools of peripheral nervous system disorders. They help in the prognosis, and monitoring of a disease process. The aim of this study is to establish the normative data of the tibial nerve among the healthy adult Sudanese population and to study the effects of age, gender, height, weight, and temperature on the obtained parameters.

Methods:: NCSs were performed in 210 tibial nerves of 105 adult healthy Sudanese subjects using standardized techniques.

Results:: It was found that the tibial nerve values were as follows; distal latency 4.063±1.0533 m/sec, proximal latency 13.238 ±1.7253 m/sec, the amplitude at ankle 8.528±3.6658 μV, the amplitude at popliteal fossa 6.343±3.2871μV, conduction velocity 48.58±5.634 m/sec, F wave 51.509±6.1013 m/sec. Duration of CMAP at ankle 6.199± 1.0254 m/sec, Area at ankle 17.569±7.7389μV/ms. Duration of at popliteal 7.075±1.3173 m/sec, and area at popliteal fossa 14.914±7.8684 μV/ms.

Conclusions:: This is the first study to establish reference values for tibial NCS in Sudan. Parameters for the tested nerve compared favorably with the existing literature with some discrepancies that were justified.
PROXIMAL WEAKNESS INVOLVEMENT IN THE FIRST ITALIAN CASE OF CHARCOT-MARIE-TOOTH
2CC HARBORING A NOVEL FRAMESHIFT VARIANT IN NEFH

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¹University of Naples Federico II, Department Of Neuroscience And Reproductive And Odontostomatological Sciences, Napoli, Italy, ²IRCCS Fondazione Stella Maris, Molecular Medicine, Pisa, Italy

Background and Aims:: Charcot-Marie-Tooth (CMT) disease is a clinically and genetically heterogeneous group of inherited sensory-motor neuropathies. In 2016, Rebelo et al. identified in two family a new causal CMT2 gene: a frameshift mutation in the neurofilament heavy chain (NEFH) gene with autosomal dominant inheritance (CMT2CC). The aim of this report is to describe the first Italian case of CMT2CC related to de novo frameshift mutation in the NEFH gene.

Methods:: The index case was a 28-year-old woman; at the age of 25 years, she developed difficulties to climb stairs and muscle weakness progressively worsened. No sensory symptoms were complained. Electrophysiological findings showed a sensory-motor axonal neuropathy, predominantly affecting the lower limbs.

Results:: In the proband, we identified the de novo heterozygous frameshift mutation c.3058_3059insT (p.K1020fs*) in the NEFH gene. The majority of patients harboring a frameshift mutation in NEFH had early and prominent involvement in proximal muscles, an unusual finding for classical length-dependent neuropathies. Conversely, the clinical phenotype was more similar to a classic, length-dependent CMT in the Chinese family harboring a missense mutation in NEFH.

Conclusions:: Type and location of mutation might influence clinical characteristics and perhaps disease progression. Under this hypothesis, frameshift variants cause a prominent involvement of hip and thigh muscles, whereas point mutations might cause a more typical length-dependent neuropathy with distal muscular involvement. NEFH-related neuropathy should be regarded as a form of CMT with proximal involvement. Red flags to assist clinicians before embarking in NGS studies include prevalently proximal muscle weakness in the legs in patients with axonal sensory-motor neuropathy.
A NEW CASE OF TRIM32/ASTN2 DELETIONS CONFIRM THE ASSOCIATION OF LMGD WITH MCI

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Background and Aims:: Defects in TRIM32 gene were reported in limb-girdle muscular dystrophy type 2H (LMGD2H). Homozygosis deletion of the entire TRIM32 gene and part of ASNT2 gene was previously described in only one patient presenting LMGD2H with a mild cognitive impairment (MCI). Interesting ASTN2 gene encodes a protein expressed in the brain and probably involved in neuronal migration. We provide an extensive phenotypic description of the second case of TRIM32/ASTN2 deletion.

Methods:: The genetic defect was detected by combined approaches of next generation sequencing (NGS) and comparative genomic hybridization (CGH) array. Muscle biopsy, electromyography (EMG), muscle and brain magnetic resonance (MRI) and neuropsychological tests supported the clinical phenotype characterization.

Results:: A 40-years-old male developed progressive weakness at limbs girdle from the age of 15. Neurological examination demonstrated weakness of scapular girdle muscles, difficulty rising from the floor, climbing stairs and walking. Serum creatine phosphokinase levels were 5 times normal. Muscle biopsy showed dystrophic changes with atrophic type I fibers. Muscle MRI proved both pelvic girdle and lower limbs involvement. Brain MRI was normal. Neuropsychological tests revealed a mild cognitive impairment. An NGS panel for LGMD did not detect pathogenetic variant but conflicting results on the TRIM32 coverage. A CGH array allowed the detection of homozygous 82 kb deletion of 9q including the whole TRIM32 gene and part of ASTN2 gene.

Conclusions:: Disruption of the ASTN2/TRIM32 should be considered in patients presenting a non-specific LMGD and a neurocognitive disease. Hence the importance of considering the roles of TRIM32 and ASTN2 in synaptic connectivity and neuronal circuits.
Background and Aims:: Pompe disease is a rare disease, known as type II glycogenesis. It is classified into two forms, the first is infantile, they manifest before the first year of life, the classic form presents with cardiomyopathy and corresponds to the most severe extreme. The second is late-onset, usually involves the extremities and the diaphragm, progressive myopathy occurs, little cardiac involvement but great involvement of the accessory respiratory muscles, which leads to relatively early respiratory failure, this being the main cause of death. the objective of this study was to describe the quality of life of a group of patients with Pompe disease.

Methods:: Descriptive cross-sectional study in 27 patients with Pompe disease. The data collection was done from March 9 to May 20, 2020 by Google Form. The Medical Outcomes Study 36-Item Short Form (SF-36) was applied.

Results:: The mean age is 40.52 years, 59% female, 51% married, 63% active in the workplace, the mean age of diagnosis was 30.3 years (SD = 15.557), 66.7% do not use a wheelchair to move around and 96.3% are on enzyme therapy.

Conclusions:: The pompe is highly disabling when it affects more in the physical dimensions, however patients can actively play their social and family role. Follow-up studies are required to demonstrate the impact of the pandemic on the application of enzyme therapy.
A CASE OF PARAMYOTONIA AND PERIODIC PARALYSIS ASSOCIATED WITH AN UNREPORTED MUTATION IN THE CACNA1S GENE

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Background and Aims:: Mutations in the CACNA1S gene are known to be associated with malignant hyperthermia, thyrotoxic periodic paralysis, hypokalemic periodic paralysis type I, and congenital myopathy, but not myotonia.

Methods:: We studied a case of overlapping episodic weakness and stiffness by using a series of assessments including medical history, physical examination, laboratory analyses, electrophysiological evaluation, MRI and genetic analysis.

Results:: We report the case of a 21-year-old man with onset at the age of 14 years of episodic painful muscle stiffness after exercise, first in the upper limbs, after a few months spread to the legs and trunk muscles, sparing the head. Two years later he began experiencing episodes of severe weakness lasting several hours, more common in cold weather, after a hard day’s work or carbohydrate-rich meal. Neurologic examination showed hyperreflexia, paradoxical myotonia and fasciculations. CPK, thyroid hormones, electrolytes levels were normal. Autoimmune disorders were excluded. EMG revealed spontaneous activity at multiple sites but not myotonia. Brain and spine MRI lacked any pathological sign. Multigene NGS analysis demonstrated a missense variant in CACNA1S p.Arg557Cys (c.1669 C>T), not previously reported in the literature, of uncertain pathological significance. Segregation analysis found the same variant in the patient’s mother, who reported a similar clinical picture, pointed to its likely pathogenicity.

Conclusions:: This is the first report of a new likely pathogenic variant of the CACNA1S gene, with a clinical phenotype combining paradoxical myotonia and periodic paralysis. Such phenotype was previously associated with variations in the SCNA4 gene, but never in the CACNA1S gene.
THYMUS CHARACTERISTICS IN SEROPosITIVE AND SERONEgATIVE MYASTHENIA GRAVIS

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Background and Aims:: Myasthenia gravis (MG) is an autoimmune disorder of neuromuscular junctions. The study of Yi Li et al. has shown that 70-85% of all patients with MG were seropositive and 8-15% seronegative. The high frequency of thymus hyperplasia in seropositive patients. Between 10% to 20% of patients with MG have a thymoma. To our knowledge, any study of MG in Mongolia has not been published yet. To study association between thymus characteristics and serological findings in patients with MG.

Methods:: We reviewed a total of 14 adult patients with MG who were diagnosed by serological findings in a five-years period from 2015 to 2020. If Acetylcholine receptor antibody level is greater than 0.40 n/L were assessed seropositive. Thymus characteristics were assessed for Chest CT scans. Statistical analysis was performed using SPSS software.

Results:: A total 14 patients had Serological tests and Computed tomography. 85.7% (n=12) patients were seropositive, 14.3% (n=2) patients were seronegative in a serological test. Thymoma in 3 cases (10% of total MG), all patients were seropositive MG. Thymus hyperplasia in 5 cases, of these 80% of patients were seropositive MG and 20% of patients were seronegative MG. No changes of thymus in 6 cases, of these 83.3% of patients were seropositive MG, 16.7% of patients were seronegative MG.

Conclusions:: Similar to other countries, the high frequency of seropositive MG in Mongolia. Thymoma rarely occurred in 10% patients who have MG.
ACUTE MYOPATHY AT ONSET OF SARS-COV-2 INFECTION

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Background and Aims:: Although various reports indicated the presence of myalgia in 44–70% and “skeletal muscle injury” (increased CK and myalgia) in 23% of hospitalized patients with SARS-CoV-2 infection, the characterization of neuromuscular involvement is still unsatisfactory, and electrophysiologic studies have rarely been performed.

Methods:: We describe a case of acute myopathy at onset of SARS-CoV-2 infection.

Results:: A 73-year-old woman, with post-infarct ischemic heart disease in her medical history, presented with progressive weakness in the lower limbs and pain, without fever. On admission, neurological examination showed proximal tetraparesis, prevalent in the lower limbs, and reflexes were diminished. CK in the serum was to >6000 U/L (normal value 10-145 U/L), hepatic enzymes were elevated (GOT 814 U/L, n.v. 1-31), urin Hb > 1 (n.v. absent). Polymerase chain reaction (PCR) testing for SARS-COV-2 was positive. Chest x-ray showed right lower patchy opacities, but oxygen saturation was 94% on room air. Motor nerve conduction studies (NCS) showed mild sensory polyneuropathy; the needle electromyography (EMG) demonstrated myopathic abnormalities with fibrillation potentials in the lower limbs, rapid recruitment on interference pattern and reduced compound muscle action potential amplitude. The therapy with high dose of steroids induced significative clinical improvement. In two weeks, CK levels almost normalized and the patient recovered the ability to walk with assistance.

Conclusions:: The severe immune activation known to occur in COVID-19 patients probably plays an important pathophysiological role for onset of rhabdomyolysis, but further studies are needed to elucidate the mechanisms, appropriate treatment, and long-term clinical outcomes of muscular manifestations associated with COVID-19 disease.

References
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ELECTROPHYSIOLOGICAL FEATURES OF GUILLAIN BARRE SYNDROME IN MONGOLIA

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Background and Aims:: Electrophysiological subtypes are important nonclinical factors to define the prognosis of patients with GBS. Many studies revealed that axonal subtype is associated with increases risks of delayed recovery, disability and mortality. It is evident that axonal subtype is higher in Asian countries. To determine the predominant electrophysiological subtype is important for treatment options. The aim of this study is to determine electrophysiological subtypes of GBS in Mongolia.

Methods:: The data was collected retrospectively from 2016 to 2019 at the Reflex Neurological Clinic. 75 patients enrolled in the study. Motor and sensor nerves were recorded on one-side using standard techniques with surface electrodes in upper and lower extremities. All statistical analyses were performed using STATA 26. The level of statistical significance was set at p<0.05.

Results:: Of 75 patients, an average age was 45±15 (18-73) and males were 44% (n=33). For antecedent events, Upper respiratory infection was 9.3%, diarrhea 21.3%, other factors 22.7%, no factors associated were 46.7%. Nerve-conduction study was evaluated with Hadden criteria, and 42.9% was classified as demyelinating (n=24), 37.5% axonal (n=21), 1.8% inexcitable (n=1), 14.3% equivocal (n=8) and 3.6% normal (n=2). Abnormal changes of demyelinating subtype were recorded in all nerves, whereas axonal subtype changes recorded clearly in N.medianus and N.Peroneus. Demyelinating and axonal subtypes were observed equally in all age groups. But axonal subtype was highly associated with disability and mortality (p<0.05). Patients with equivocal and normal ENG features were not reassessed further.

Conclusions:: In Mongolia, demyelinating subtype was predominant however axonal subtype remained higher.
THYMECTOMY IS THERAPEUTICALLY BENEFICIAL FOR PATIENTS WITH MYASTHENIA GRAVIS IN EAST AFRICA: A CLINICO-DEMOGRAPHIC STUDY OF 85 CASES

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Background and Aims:: There are very few studies from sub-Saharan Africa on myasthenia gravis (MG), with some evidence from South Africa that the disease differs from global trends. This has never been quantified in East Africa. We therefore sought to describe the clinical features, treatment strategies and disease course in MG patients referred to our tertiary regional neurology centre.

Methods:: In a retrospective study covering the period 2009-2019, we captured clinical data of MG patients, and recorded clinical status using the Myasthenia Gravis Foundation of America (MGFA) classification. We sub-analysed the therapeutic effects of thymectomy.

Results:: In n=85 [male=56.5% (48/85); mean age 49.6 years], 30.6% (26/85) had ocular MG (MGFA class 1), and 69.4% (59/85) had generalised MG, of which (at onset) 72.8% (43/59) had mild/moderate (class II/III) disease. Average time to diagnosis was 3.0 months. 36.1% (30/85) had a thymus, and were significantly (p<0.05) more likely to have: anti-acetylcholine receptor antibodies (89.7% vs 57.4%); generalised MG (93.1% vs 50.9%); early immunosuppression requirements (96.6% vs 76.8%); and more relapses (79.3% vs 44.6%). 29/30 underwent thymectomy. resulting in: (i) significant (p<0.05) median dose reduction of pyridostygmine (240mg to 90mg) and prednisolone (25mg to 5mg) by last follow-up [non-thymectomy patients required significantly higher median doses (pyridostigmine 181mg, prednisolone 9mg)]; and (ii) improvement by ≥1 class of MGFA in 96.5% (28/29), with 24 becoming asymptomatic and 2 achieving complete remission requiring no medication.

Conclusions:: Our cohort’s disease characteristics follow global trends: thymectomy leads to reduction in immunosuppression with better symptom control, and should therefore be standard of care in eligible patients.
NORMATIVE DATA FOR LOWER LIMB NERVE CONDUCTION STUDIES IN MONGOLIA

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Background and Aims:: Nerve conduction study is widely used to diagnose peripheral nerve diseases. Normative data is essential part of the evaluating the abnormality, therefore most individual laboratories use their own techniques and reference data. We aimed to provide normative electrophysiological data for lower limb nerves in normal healthy adults in Mongolia

Methods:: Nerve conduction studies were performed in lower limbs of 69 healthy adults using standardized techniques. The peroneal and tibial nerves met the NDTF criteria. Nihon Kohden Neuropack S1 machine was used.

Results:: A 69 healthy subjects were investigated, female 47.8% and male 52.2%, age ranged 18-71. Mean onset latencies were 3.8 ±0.6 and 4.1±0.8 ms, amplitudes were 4.2±2.1 and 12.6±4.3 mV, and conduction velocities were 50.8±5.2 and 45.3±5.5 ms for peroneal and tibial motor nerves, respectively. Also, minimal latency of F waves were 46.4±3.9 ms, 46.7±4.0 ms, side to side difference were 1.8±1.2, 1.2±1.0. As H reflex, H latency was 31.08±3.06, M latency was 4.3±0.84, and H/M ratio was 0.3±0.3. In sensory nerves, mean onset latencies were 2.7±0.8 and 2.4±0.4 ms, mean amplitudes were 7.2±3.9 and 16.6±9.1 µV, and mean nerve conduction velocities were 45.3±8.2 and 49.7±8.3 ms for superficial peroneal and sural nerves, respectively. Peroneal motor conduction velocity in females higher than males, whereas tibial sensor latency in females shorter than males. Peroneal sensor amplitude in BMI<24.9 higher in BMI>25. Latency to the peroneal and tibial increased with increasing height.

Conclusions:: Our study results are similar to those data published in the literature. Also, we should be considering demographic factors in NCV.
COMPARISON OF PREVALENCE AND RISK FACTORS FOR PERIPHERAL NEUROPATHY BETWEEN PATIENTS WITH HIV INFECTION AND PATIENTS WITH CONCURRENT HIV AND DIABETES MELLITUS

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Background and Aims:: The ageing population living with HIV is predisposed to non-communicable comorbidities, including diabetes. Peripheral neuropathy (PN) can occur in both conditions, and it is thought co-existence of both illnesses has a synergistic impact on PN. We sought to identify the prevalence of PN in our population of patients with HIV infection compared with those with both HIV and diabetes.

Methods:: We undertook a prospective cross-sectional study at tertiary regional referral hospital. We collected demographics, duration of treatments and disease characteristics. PN symptoms was assessed by the Neuropathy Symptom Score and examined using the Neuropathy Disability Score and monofilament testing.

Results:: We recruited 68 patients in either group; 55% were males, and median age was 51 years. Overall median duration for HIV was 10 years with median CD4 count of 524 cells/mm³ and for HIV/diabetes group average 3.85 years since diabetes diagnosis with a mean HbA1c of 7.65%. 67% of patients had suppressed viral loads, and 9 patients (6.6%) had history of neurotoxic anti-retroviral therapy use. PN was detected in 11 (16%) HIV-only patients, and in 17 (25%) participants who had both HIV and diabetes (Fisher exact test and corrected chi-square=0.4). In univariate analysis, old age, high BMI and long duration of HIV were associated with OR of 1.07, 1.21 and 1.07 in the overall group, respectively.

Conclusions:: The analysis of our study revealed slightly higher but non-significant prevalence of PN in patients with both HIV and diabetes when compared to HIV alone. HIV disease control had no association with development of PN.
Background and Aims:: In the last decades, there has been a steady increase in the frequency of late-onset (≥50 years-of-age) myasthenia gravis (MG). Recently, the so-called very late-onset MG (VLOMG, onset ≥65 years) was reported as the most common disease subtype. We investigated the demographic changes over two decades and VLOMG characteristics in a single-centre cohort.

Methods:: Patients with onset between 2000 and 2020 were included. AChR and MuSK antibodies (Abs) were tested by standard RIA. We recorded clinical data and Ab status, and compared the demographics of MG patients with onset in the first (2000-2009) vs. the second decade (2010-2020).

Results:: Our study included 674 patients (333/674 females, 49%): 567 AChR-Ab positive, 54 MuSK-Ab positive and 53 double-seronegative patients. MG onset peaked between 65 and 69 years of age through the whole observation period. In the last decade, we observed a sharp increase in the proportion of VLOMG cases (p<0.0001) paralleled by a significant rise of male frequency (p<0.0001). The VLOMG subtype mostly consisted of AChR-Ab positive cases. Only 6/54 (11%) MuSK-Ab positive patients had VLOMG, 5/6 with disease onset in the last decade. Compared to late-onset MG, VLOMG was characterized by a very high AChR-Ab positivity rate (95.6% vs 84.1%,p<0.0001), and a reduced association with thymoma (12.7% vs 29.4%,p<0.0001).

Conclusions:: In the last decade, VLOMG has become the larger disease subtype. The high rate of AChR-Abs we found in VLOMG facilitates its diagnostic confirmation. Our study provides diagnostic clues that aid the recognition of MG in the elderly.
Background and Aims: Background: Myasthenia gravis (MG) is an autoimmune disorder caused by antibodies to the muscle acetylcholine receptors (AChRs) at the neuromuscular junction.

Objectives: To study the demographic, clinical features and drug prescribing pattern of patients with myasthenia gravis in Penang hospital.

Methods: This is a cross-sectional retrospective study. Data were collected from the database from neurology clinic Penang hospital from 1976 to 2012.

Results: Findings: 186 myasthenia cases were identified. 55% were females. Majority were Chinese (58%) compared to Malays (32%) and Indians (10%).

Mean age at onset was 46 years.

Ocular symptoms were the most commonly seen as initial presenting symptoms. 100 patients (54%) with Osserman grade I at onset, 33 with Osserman GIIA, 42 with Osserman GIIB, 7 with grade III at onset.

20% of patients had thymectomy.

11% of patients had history of myasthenic crisis with ICU stay requiring IVIG during the course of illness.

51 MG patients has concurrent DM, 35 patients has concurrent HPT, 12 patients asthma, 4 patients has Graves or thyrotoxicosis.

Conclusions: Conclusion: Our study showed that MG has female predominance, similar to world data.
MOLECULAR DIAGNOSIS OF DUCHENNE MUSCULAR DYSTROPHY: SYSTEMATIC REVIEW AND META-ANALYSIS.

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Background and Aims:: Duchenne Muscular Dystrophy (DMD) is a disease caused by a mutation in a gene linked to the X chromosome, that produces dystrophin. Its diagnosis is based in your detecting, it is possible to use different techniques such multiple ligand-dependent probes (MLPA) and new sequencing generation (NGS) among others. We aimed to know the accuracy of this methods.

Methods:: A systematic review about the genetic diagnosis for DMD using MLPA and NGS were done. A search was performed in PubMed/Medline and Scopus, the quality was assessment with Quadas-II instrument and the certainty with GRADE system. Meta-analysis were performed to estimate accuracy indicators such sensitivity, specificity or detection rate (true positives of all confirmed patients). The univariate random-effects model was used and heterogeneity was assessed with I-squared(I2), while publication bias with funnel plot and Egger's test.

Results:: For MLPA, with 10 observational studies we estimate a sensitivity of 0.80(95%CI:0.76-0.84, I-square:86.48) and specificity was 0.93(CI 95%: 0.87-0.96, I2:47.27). For NGS, with 14 observational studies we estimate a DR of 73.17(95%CI:60.46-85.88, I-squared:95.96%). Also, with 10 observational studies (n=3958) of cases evaluated by NGS in patients with clinical suspicion and negative DMD for MLPA, the DR was 94.73 (95%IC:92.34–97.11, I-squared: 95.41%)

Conclusions:: With moderate and small certainty, in patients with DMD’ suspicion, the MLPA test has a very precise sensitivity and specificity to establish the diagnosis and the NGS test has a detection rate moderate, and in who have an MLPA result negative (18to20%), the application of NGS adds a 73% detection rate, which would reach 95% of detected cases.
LEWIS-SUMNER SYNDROME WITH LOWER-LIMB ONSET: UN UNDER-RECOGNIZED ENTITY

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Background and Aims:: Lewis-Sumner syndrome (LSS) is an atypical form of chronic inflammatory demyelinating polyneuropathy (CIDP) with clinical phenotype of asymmetric motor and sensory disturbances with initial involvement and more prominent presentation in the arms. However, some of these patients may have lower-limb onset, making the diagnosis more challenging. The aim of our study was to estimate the prevalence of lower-limb onset patients with LSS and define their clinical features. Methods:: We collected data from 32 medical charts of patients with LSS. All the patients satisfied at least “probable” criteria EFNS/PNS, 2010. Results:: We evaluated that 15/32 (46%) of the patients presented with lower-limb onset. 4/32 (12%) had only lower-limbs involvement at the time of diagnosis. All of them had an asymmetrical deficit. The mean time of the diagnosis in patients with symptoms only in the lower limbs was 10[3;12] vs 3[1;11] years (p<0,05). Nerve conduction study (NCS) of the lower limbs was lacking demyelinating features and interpreted as primary axonal in all patients. Only additional investigation of the upper extremities led to the diagnosis. Complementary investigation with nerve ultrasound revealed changes only in the upper extremities. Conclusions:: We demonstrated the high prevalence of LSS with lower-limb onset. Noteworthy, that some of the patients may have isolated clinical distribution in the lower limbs. This should raise the suspicion of LSS and highlight the importance of complex NCS of the upper and lower extremities in all patients with asymmetric neuropathy. We also found that nerve ultrasound of the lower extremities in LSS has limited significance.
A LATIUM REGION REGISTRY ON AMYOTROPHIC LATERAL SCLEROSIS

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Background and Aims:: In 2016 a pathology registry of ALS was established in Latium (LaRALS) , a central region of Italy . The aim of the study was to describe the clinical and socio-demographic characteristics of patients enrolled in LaRALS, and to analyse possible gender differences.

Methods:: The LaRALS was conducted with a network of clinical centers, throughout the adoption of an information form filled . Data from ALS participants were analyzed to determine characteristics, such as site of onset, time of symptom onset to diagnosis, diagnostic level, education level, ALSFRS-R and BMI at visit, life-style and risk factors.

Results:: Between july 2016 and march 2017 were included in the LaRALS 353 patients, 200 males and 153 females, mean age at prevalence and disease onset was 66 ±11.1 years and 61.6 ± 11.9 years, respectively. The 60.9% of patients had a spinal onset, 26.6% bulbar onset and 8.2% generalized onset. The mean diagnosis delay for bulbar onset patients was 0.9±1.3 years, for spinal onset was 1.8±2.3 years and 1.1±1.2 years for generalized onset. The multivariate logistic analysis for female vs male showed an associaton statistically significant in bulbar site onset respect to spinal, BMI at visit, and some risk factors (smoking status, history of alcohol consumption, sport activity).

Conclusions:: The clinical and sociodemographic characteristic of patients included in the LaRALS are similar to patients included in other registries. The pathology registry could establish a better characterization of clinical form at site onset and gender differences in ALS.
SMALL VOLUME PLASMAPHERESIS: A CHOICE FOR GUILLAIN-BARRE SYNDROME’S TREATMENT

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Background and Aims:: Plasma exchanges and intravenous immunoglobulin have proven to be effective in accelerating motor recovery in GBS. Developing countries as Morocco are often limited by the cost of treatment and the unavailability of substitute products. We report our experience to highlight the usefulness of small volume plasmapheresis (SVP) in the treatment of GBS. A technique based on nanofiltration without the use of substitutes which are limited by donors’ availability.

Methods:: The study was conducted without a commercial relationship and with respect for the ethical conditions. The study recruited 50 patients hospitalized in the neurology department of the Mohamed VI University Hospital of Marrakech for GBS according to the Brighton criteria. Patients received 5 sessions of SPV over 10 to 14 days. The efficacy evaluated by the evolution of the Hughes and MRC sum scores one month after the treatment, the use of mechanical ventilation, the mortality rate and the length of hospital stay.

Results:: We found that the mean MRC sum score increased from 29.8 ±13.1 to 45.4 ±15.3, the mean Hughes score increased from 3.7 ± 1.0 to 2.1± 1.6, the improvement in the MRC sum score was 15.6 and 84% of patients increased one or more grades on Hughes and MRC scores after one month of progression. Mechanical ventilation was required in 17.2 % with a mortality rate of 6.2 %, and the mean length of hospital stay was 15.4 ±5.1 days.

Conclusions:: SVP is an alternative for the treatment of GBS that can be used easily with a significant clinical improvement.
SPINAL MUSCULAR ATROPHY TYPE II WITH HYBRID SMN GENE: A CASE REPORT

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Background and Aims:: Spinal muscular atrophy (SMA) is a neuromuscular disease with homozygous deletion of SMN 1 exons 7 and 8. In 5 to 30% of all SMA patients, exon 8 was retained and forming a hybrid SMN gene.

Methods:: Case Report

Results:: We report a 19-year-old female who presented with frequently fall when walking and had difficulty standing up again, since she was 1-year-old; suggested that she has SMA Type II. The ability to walk then gradually decrease; she totally could not stand and walk at 11-year-old. The weakness of upper extremities began at 14-year-old. Her older brother has the same weakness and died at 17-year-old. Neurological examination showed that the weakness was flaccid tetraparesis dominantly proximal part of the extremities. Scoliosis were found with Cob angle 71.4 degree. CK level and spirometry was normal. EMG examination showed axonophaty in motor nerve and preservation of sensory nerve, supporting the lesion in anterior cornu of the spine. Genetic examination showed that in SMN 1, exon 7 was deleted but exon 8 still remain. Usually patient with SMA type II could only sit, but in this patient she could stand and walk as highest motor milestone achievement.

Conclusions:: SMA patient with hybrid SMN gene has milder clinical manifestation and better life expectancy.
ASSOCIATION OF ALBUMIN, SODIUM AND POTASSIUM LEVELS WITH THE OUTCOME IN PLASMA EXCHANGE TREATED GUILLAIN BARRE SYNDROME

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Background and Aims:: Guillain Barre Syndrome (GBS) is an autoimmune neuromuscular disease characterized by the acute progressive weakness, with the complication of respiratory distress. It is important to look for appropriate biomarker to predict the outcome of GBS. In this study, we assess three parameters: albumin, sodium and potassium, to know whether there is an association with the outcome of GBS patients.

Methods:: This cohort retrospective study used serum samples during admission from 66 GBS patients, hospitalized in public hospital Yogyakarta, treated with plasma exchange. The study started from January 2015 through November 2020. The clinical outcome was muscle weakness (measured by Medical Research Council sum score) at discharge.

Results:: Three parameters, albumin, sodium and potassium levels were measured (mean [SD] age 29.83 [17.99] years old; 40 males [60.6%] and 26 females [39.4%]; demyelination 33 [50%] and axonal 22 [50%]). During admission, the parameters level were (mean mmol/L [SD]) albumin 4.01 [0.51], sodium 137.39 [4.08], potassium 3.9 [0.42]. All patients were treated with plasma exchange with the mean number 5.45 times (SD 1.17). The association of these parameters with MRC sum score at discharge were albumin (r= -0.064, P=0.609), sodium (r=0.118, P=0.344) and potassium (r= -0.113, P=0.368). There were no significant association between albumin, sodium and potassium levels at admission with the MRC sum score at discharge.

Conclusions:: Albumin, sodium and potassium levels may not associate with the outcome of plasma exchange – treated GBS. It is important to study another parameters as biomarker to predict the outcome of GBS patient.
EATON LAMBERT SYNDROME (LEMS) IS A DIAGNOSTIC CHALLENGE AND STIMULATED SINGLE FIBER ELECTROMYOGRAPHY (SSFEMG) IS OFFERING A GREAT ROLE IN ITS EARLY DIAGNOSIS.

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Background and Aims:: LEMS is a presynaptic neuromuscular disorder, its early recognition is particularly important because of its strong association with small cell lung cancer (SCLC) and up to 50% are misdiagnosed. LEMS is often suspected according to symptoms. Electrodiagnostic approach includes Routine motor nerve conduction stimulation typically elicits a small amplitude compound muscle action potential (CMAP), with its increase >100% increment after After isometric contraction for 10 seconds, or high rate repetitive supramaximal stimulation, but what if it increases but not reaching 100%?

Methods:: SSFEMG is a neurophysiological test to study the neuromuscular junction & allows stimulation rate control. That shows the typical rate-dependent reduction of the neuromuscular jitter and blocking in LEMS compared to MG that show more prolongation of jitter and even more blocking. This is a case study for a 50 year-old woman presenting with proximal and axial weakness, lately developed bilateral ptosis, and symptoms compatible with an autonomic dysfunction, electrophysiologically she showed nonsignificant increments but showed typical rate-dependent reduction of the neuromuscular jitter and blocking reduction.

Results:: The patient was diagnosed to have lung cancer and Diagnosis was confirmed by serological demonstration of circulating VGCC antibodies after diagnosis by typical rate dependent SFEMG findings.

Conclusions:: Early recognition of LEMS is particularly important because of its strong association with cancer, it may serve as a marker for early disease, and thus allow more effective treatment of malignancy and rate dependent SSFEMG offered a useful tool for the early diagnosis.
MICRO-RNA-206 LEVEL IS INCREASED IN FAST EVOLVING TRANSPORTINOPATHY (LGMD-D2), CALPAINOPATHY (LGMD R-1) AND SARCOCGLYCANOPATHY (LGMD R3-R5)

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Background and Aims:: Limb-girdle muscular dystrophies (LGMD) are clinically and genetically heterogeneous conditions presenting with a wide clinical spectrum leading to progressive proximal weakness caused by loss of muscle fibers. LGMD are presenting with various phenotypes, high CK, leading to muscle degenerative features at muscle MRI. MiR-206 is a member of myomiRs, a group of miRNAs with important functions in skeletal muscle. The aim is to determine the value of miR-206 in detecting muscle disease evolution in LGMD. We described clinical features, disease history, and progression of eleven patients affected by LGMD subdivided into Transportinopathy, Sarcoglycanopathies, and Calpainopathy subtypes.

Methods:: In 11 Calpainopathy trasportinopathy and sarcoglycanopathy cases clinically diagnosed we performed a clinical examination and scored them to evaluate disease progression. In undiagnosed cases, the patients’ mutations were identified and in all, we studied the circulating miR-206 in serum by qRT-PCR, muscle MRI was done with 1.5 Tesla Philips apparatus.

Results:: The evolution/progression of disease was associated with the expression levels of miR-206, which was significant elevated in severe evolving LGMD patients in comparison with a control group. In particular, we observed an overexpression of miR-206 of 50-80 folds in two patients: one child affected by early-onset transportinopathy, one juvenile calpainopathy patient with a severe and fast course of the disease. The muscle substitution and changes were documented by muscle MRI.

Conclusions:: Evolutive changes were documented by muscle MRI. This study provides the first evidence that miR-206 was associated with severe phenotypic expression and it could be used as a prognostic indicator of LGMD disease progression.
EARLY ONSET CALSEQUESTRIN DEFECT: A NEW PHENOTYPE WITH LIMB ASYMMETRY.

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Background and Aims:: Calsequestrin (CASQ) represents the main Ca2+ buffer in the sarcoplasmic reticulum. The CASQ1 and CASQ2 isoforms are preferentially expressed in skeletal and cardiac/smooth muscle, CASQ1 is largely predominant in fast-twitch (type II) fibers. CASQ1 buffers Ca2+ and prevents it from precipitating, maintaining large-capacity gradient release large amounts of Ca2+ on stimulus. The first human myopathy associated with CASQ1 mutations was only recently reported: a founder mutation (c.731A>G, p.Asp244Gly) was first described in patients presenting a non-debilitating vacuolar myopathy, we report an early-onset case with the same mutation, but early-onset new phenotype.

Methods:: The index case had high CK, at 9 years, at 11 years she complained of myalgia, fatiguability, limb asymmetry, winging scapulae. The elevated CK was present in her mother, that like the grandmother had a clubfoot at birth and sister that complained of myalgia. A biopsy was done and showed few vacuoles and some atrophic, degenerating regenerating fibers and analyzed by NGS, which showed in chromosome 1 the CASQ1 mutation in exon 6:cA731G:pAsp244Gly.

Results:: The patient suffered from limb asymmetry, was operated on by shortening of the right femur and elongation of the contralateral limb, but still had elevated CK and easy fatiguability. The muscle biopsy showed some atrophic fibers and vacuoles, but a definite diagnosis came from NGS, which revealed the pathogenic mutation.

Conclusions:: We interpret the asymmetric limb myopathy as a result of somatic mosaicism, resulting in different biodistribution of its effects, likely this entity is underdiagnosed, although high CK and vacuolated fibers at biopsy might suggest the diagnosis.
GUILLEIN-BARRE SYNDROME AFTER CORONARY ARTERY BYPASS GRAFT SURGERY: A CASE REPORT AND LITERATURE REVIEW

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Background and Aims:: Guillain-Barre syndrome (GBS) is an acute polyradiculoneuropathy, often preceded by an infection. Rarely, it is preceded by a surgical procedure. Most of the postsurgical GBS cases are reported with neurosurgical, gastrointestinal, orthopedic, and cardiac procedures. GBS is rarely reported after coronary artery bypass grafting (CABG). To date, only 12 cases have been reported in the literature. Our case is 13th in number and the first case from Pakistan.

Methods:: We report a case of a 54-year-old man who presented with acute flaccid quadriparesis and areflexia after a CABG procedure.

Results:: He was subsequently diagnosed with an acute inflammatory demyelinating polyneuropathy (AIDP) variant of GBS and underwent five sessions of plasmapheresis. His weakness improved and could ambulate unassisted on follow-up visits.

Conclusions:: GBS is a potentially treatable condition if timely diagnosed and managed. It should be considered in every patient presenting with an acute-onset weakness after surgery.
A VERY RARE CASE OF PURE SENSORY GUILLAIN BARRE SYNDROME WITH AXONAL FEATURES

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Background and Aims:: Pure sensory Guillain-Barré syndrome “GBS” is controversial. Case reports of the condition are scarce, and most were due to acute demyelination of peripheral sensory nerves. Cases secondary to axonal damage is rarer and overlap with sensory neuronopathy.

Methods:: We report a rare case of pure sensory GBS following primary Varicella Zoster infection (VZV).

Results:: A 31-year-old lady with recent primary VZV infection presented with acute sensory symptoms and signs of her trunk and limbs, without weakness. Examination showed severe impairment of all sensory modalities in limbs and trunk, pseudo-athetoid movements, sensory ataxia, positive Romberg’s sign, and areflexia. She could not stand or walk. CSF analysis showed albuminocytological dissociation. MRI of the spine with contrast showed multiple root enhancement. Nerve conduction studies “NCS” demonstrated absent sensory action potentials, with normal motor nerves responses. Initial electromyography was normal. After differential diagnoses were appropriately excluded, most importantly sensory neuronopathy, the patient was diagnosed with pure sensory axonal GBS and treated with IVIG for five days. She improved gradually. Her sixth month GBS disability score was two. Follow-up NCS was unchanged, but repeated EMGs revealed denervation potentials in multiple levels, suggesting a subclinical axonal motor involvement and excluding sensory neuronopathy.

Conclusions:: This case illustrates the difficulties in diagnosing pure sensory GBS and the significance of early treatment. It also demonstrates the value of follow-up EMGs in excluding sensory neuronopathy as an important differential diagnosis. Finally, clinical improvement is not necessarily reflected in sensory NCS findings.
ELECTRIC LESION MONONEUROPATHY

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Background and Aims:: Electricity can provoke a great variety of lesions in the human body. In the neurologic field, both the peripheral nervous system, as the central nervous system can be involved. High voltage discharges are the most dangerous.

Methods:: We expose a case report

Results:: A 34-years-old woman consulted us two months after suffering an electric accident with a machine connected to high tension current (she worked as a radiodiagnosis operator). She referred that in a first moment, she suffered a little burn injury with a painful sensation in her entire arm. Since that moment, she experiences dysesthesia, allodynia and weakness in the right median nerve territory. In the neurologic examination, we detected weakness in the muscles innervated by the right median nerve. The rest of the examination was normal. In the electroneurography, we detected a nerve conduction blockade in the right median nerve. We requested a magnetic resonance image (MRI) of this limb, in order to discriminate soft tissue inflammation, that was normal.

Conclusions:: The nervous system has a very low electric resistance, so it is very vulnerable to be damaged in electric accidents, sometimes in an irreversible way. These kinds of lesions can be due to alteration of the electric conductivity because of coagulative necrosis of the nerve, or because of myelin sheath damage. Another possible cause is the compression of the vasa nervorum because of edema and compartment syndrome. This last possibility was discarded in our patient with a MRI.
Background and Aims:: To determine the frequencies of electrophysiological variants of Guillain-Barre’ Syndrome and the outcome of each in Sudanese adult patients diagnosed with GBS in the period from March 2020– September 2020

Methods:: a prospective study of a 62 patients with GBS. The study was conducted in the period from March – September2020, in a 4 neurology centers in Khartoum. All patients were adults sudanese, Seen and diagnosed with GBS by a consultant neurologist All have done nerve study. That have been reported by expert electro-physiologists. All patients were seen and examined by the researcher at the disease nadir and followed at day-30 from disease onset by phone to determine the grade of HFGS.

Results:: Males are and females are equally represented, the majority of patients (70%) are between 18 years and 50 years. The onset of the weakness was less than or equal 3 days in (33.9%) of patients, from 4 to 7 days in (41.9%) , from 8 to 14 days in (11.3%) and above 14 days in (12.9%). Based on the electrophysiology, (37.09%) were classified as (AMAN), (29.03%) as (AIDP) and (29.03%) as (AMSAN). 30 patients (48.4%) fully recovered, 25 patients (40.3%) recovered with motor deficit, and 7 patients (11.3%) died.

Conclusions:: Axonal type of GBS found to be in nearly 2/3 patients. Age of the patients, onset of the disease and dysautonemia did not show statistically significant effect on outcome at day-30. The outcome of axonal types at day-30 was poorer than that of demyelinating form
DAYTIME SLEEPINESS IN MYOTONIC DYSTROPHY TYPE 1 IN TUNISIAN POPULATION

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Background and Aims::

Excessive daytime sleepiness (EDS) is the most frequent non-muscular disorder in DM1, being present in about 70-80% of patients. It may be one of the earliest symptoms of DM1. Several patients present EDS many years before DM1 is diagnosed.

Methods:: The study was conducted in the department of neurology Hbib Bourguiba sfax between June 2009 and December 2019. Daytime sleepiness was assessed with the Daytime Sleepiness Scale (DSS) which was developed specifically to measure the degree of daytime sleepiness in patients with DM1. It is a score that varies from 0 to 15. It is considered indicative when it is ≥ 7. All patients had clinical and psychiatric evaluation and cerebral MRI.

Results::

We included twenty individuals (9 females, 11 males) with DM1 genetically confirmed (mean age 40 y, range 28-49 y). Half of our patients had EDS. The mean age of onset of the disease was 27 year-old. We did not find significant relationships between the DSS score, age of onset of the disease, motor disability, cerebral MRI lesions, or cytosine-thymine-guanine (CTG) repeats (p=0.5). We found a significant relationship between the DSS score and depression (p= 0.04).

Conclusions:: DM1 patients with EDS present higher levels of depressive symptoms than those without EDS. Some authors consider it to be a Central nervous system disease although the non correlation between MRI lesions and EDS in our patients. The EDS, always misdiagnosed, seems to affect the quality of life of patients with DM1.
Background and Aims:: Myotonic dystrophy type 1 (DM1) is the most frequently inherited neuromuscular disease. Although relatively frequent, very limited data exists about psychiatric phenotypes in the adulthood form. The aim of this study was to investigate the psychiatric phenotype in individuals with DM1.

Methods:: The study was conducted in the department of neurology Habib Bourguiba sfax between June 2009 and December 2019. Depression and anxiety have been searched thanks to the Arabized Hospital Anxiety and Depression Scale (HADS). This scale includes 14 items rated from 0 to 3. Seven questions are related to anxiety (total A) and seven others to the depressive dimension (total D), allowing two scores to be obtained. The diagnosis of DM1 was genetically confirmed in all patients.

Results:: We included twenty DM1 patients (mean age 40 y, range 28-49y). Seventy five percent of patients had a score less than 7. Twenty five percent of patients had doubtful anxiety and twenty five of patients had a suspicious depressive syndrome. Neither depression nor anxiety correlated with the sex, age of onset of the disease, endocrine disorders or with CTG repeat numbers. Depression was correlated with motor disability and daytime sleepiness.

Conclusions:: Anxiety disorders have been little studied compared to mood and personality disorders in DM1. Although its non correlation with depression, these troubles may be strongly related and conduce to difficulty in social integration. Depression was related to motor disability, occasioning reciprocal worsening and hindering the progressive course of the disease. These disorders should be considered since they can be improved through psychotherapy and social skills training.
Background and Aims:: Neurophysiological patterns in patients with foodborne botulism are rarely described after the acute phase. We report data from a large Italian outbreak of botulism, with patients evaluated at different timepoints after poisoning.

Methods:: Eighteen male patients (mean age 47 ± 8.4 years) underwent 22 clinical and neurophysiological evaluations (4 patients were re-evaluated). The resting compound muscle action potential (CMAP) amplitude, postexercise CMAP amplitude, CMAP change after high-frequency (50 Hz) repetitive nerve stimulation (HFRNS), and motor unit action potentials (MUAPs) were assessed in the acute (4–8 days after poisoning; 5 patients), early post-acute (32–39 days after poisoning; 5 patients), and late post-acute (66–80 days after poisoning; 12 patients) phases.

Results:: In the acute, early post-acute, and late post-acute phases, respectively, reduced CMAP amplitudes were found in 100%, 20%, and 17% of patients; abnormal postexercise CMAP facilitation was observed in 100%, 40%, and 0% of patients; and pathological incremental responses to HFRNS were found in 80%, 50%, and 8% of patients. Baseline CMAP amplitudes, postexercise CMAP facilitation, and CMAP increases in response to HFRNS differed significantly between the acute and post-acute phases. Small MUAPs were found in 100% of patients in the acute and early post-acute phases and in 50% of patients in the late post-acute phase.

Conclusions:: The neurophysiological findings of foodborne botulism vary considerably according to the evaluation timepoint. In the post-acute phase, different neurophysiological techniques must be applied to support a diagnosis of botulism.
QUALITY OF LIFE IN PATIENTS WITH CARPAL TUNNEL SYNDROME

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Background and Aims:: Though carpal tunnel syndrome (CTS) is a focal neuropathy, it causes significant distress while carrying out simple day-to-day activities, hinders professional work, and contributes to absenteeism. However, limited studies have systematically evaluated the quality of life (QoL) in CTS. We aimed to study QoL in patients with CTS and correlate with clinical severity.

Methods:: In this prospective cross-sectional study, 44 patients attending the out-patient department of a single neurology unit, diagnosed to have CTS by the American Association of Electrodiagnostic Medicine criteria, were assessed using the 36-Item Short Form Health Survey questionnaire (SF-36). Age and gender-matched healthy subjects were recruited as controls.

Results:: There were 36 women, mean(±SD) age was 43.0±8.6 years, and mean(±SD) symptom-duration was 23.13±25.3 months. Mean(±SD) SF-36 scores in domains of Physical functioning, Role limitations due to physical health, Role limitations due to emotional problems, Energy/fatigue, Emotional well-being, Social functioning, Pain, and General health were 73.97±13.6, 43.24±38.0, 90.12±22.0, 74.59±12.4, 87.13±8.2, 65.39±19.9, 64.14±23.9, and 56.22±15.6 respectively. In all these specified domains, except for emotional well-being, the scores were lower in patients than controls (p<0.05). Total SF-36 score was significantly worse in patients than controls (p=0.0001). SF-36 scores correlated with pain rating by visual analogue scale (p=0.003), and with clinical severity, as assessed by the functional severity scale and symptom severity scale components of the Boston CTS questionnaire (p<0.0001).

Conclusions:: Poor QoL correlates with clinical severity of CTS which may adversely affect work efficiency. It is important that the treatment of CTS also address improvement in these domains.
DOUBLE-BLINDED, RANDOMIZED, PLACEBO-CONTROLLED PHASE 2 STUDY OF FCRN ANTAGONIST BATOCILMAB IN CHINESE GENERALIZED MYASTHENIA GRAVIS

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Background and Aims:: To evaluate the clinical efficacy and safety of batocilmab as a novel anti-FcRn therapy for generalized myasthenia gravis (gMG) in Chinese population.

Methods:: 30 gMG subjects (AChR Ab+) were randomly assigned (1:1:1) to received 6 doses of batocilmab 340 mg, 680 mg, or placebo once weekly combined with their standard-of-care therapy. Primary endpoint was Myasthenia Gravis Activities of Daily Living (MG-ADL) score changes from baseline on Day 43. Secondary endpoints included assessment on Quantitative Myasthenia Gravis (QMG), Myasthenia Gravis Composite (MGC), Myasthenia Gravis Quality of Life (MG-QoL), pharmacokinetics, pharmacodynamics and safety events.

Results:: Batocilmab treatment groups demonstrated significant MG-ADL score improvement on Day 43, by -4.7±0.6 (340 mg) and -4.4±1.0 (680 mg), respectively, compared with -2.2±0.9 (placebo); All 4 efficacy scales consistently demonstrated clinical improvements with robust IgG reduction (-57% and -74% for 340 mg and 680 mg, respectively). Batocilmab treatment groups showed: higher proportion (57.1% vs 33.3%) of early responder (2 points improvement in MG-ADL achieved in 2 weeks after 1st dose); and more subjects (33.0% vs 11%) of minimal symptom expression (MG-ADL 0 or 1 point). Batocilmab was well-tolerated, with treatment-emergent adverse events (TEAEs) balanced across 3 groups, no serious adverse events or AEs leading to discontinuation.

Conclusions:: Batocilmab demonstrated favorable efficacy/safety profiles, with fast, substantial, and persistent clinical improvements in Chinese gMG.
SLEEP QUALITY AND ITS CORRELATION WITH CLINICAL SEVERITY IN CARPAL TUNNEL SYNDROME

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Background and Aims:: Nocturnal pain and paresthesias are hallmark of carpal tunnel syndrome (CTS) and they commonly disturb sleep. However, there is limited literature on the nature of sleep disturbances in CTS, even though this is the commonest neuropathy. We aimed to systematically analyze sleep quality in CTS and correlate with the clinical severity.

Methods:: Prospective cross-sectional evaluation of patients diagnosed to have CTS by the American Association of Electrodiagnostic Medicine criteria from a single neurology unit was carried out using Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS) and Insomnia Severity Index (ISI). Clinical severity was assessed using visual analogue scale (VAS) for pain and Boston CTS questionnaire [functional severity scale (FSS) and symptom severity scale (SSS)]. Age and gender-matched healthy subjects were recruited as controls.

Results:: There were 44 patients (M: F 1:4.5, mean(±SD) age: 43.0±8.6 years, mean symptom-duration: 23.13±25.3 months). Mean(±SD) PSQI and ESS were 6.32±2.6 and 4.55±3.7 respectively. Thirty-three (75%) patients were classified as poor sleepers (PSQI≥5). Patients had worse mean PSQI and ESS than controls (p<0.05). Mean ISI was higher in patients than controls (p<0.0001). Significant correlations were noted between PSQI and VAS (r=0.434), PSQI and FSS (r=0.431), PSQI and SSS (r=0.507), ESS and FSS (r=0.358), ESS and SSS (r=0.416), ISI and VAS (r=0.411), ISI and FSS (r=0.429), ISI and SSS (r=0.56).

Conclusions:: Patients with CTS had poor subjective sleep quality with reduced overall sleep duration, increased sleep latency, frequent awakenings, and increased daytime sleepiness. Sleep quality was worse in those with higher grades of clinical severity.
MG-LEMS OVERLAP SYNDROME ASSOCIATED WITH MUSK ANTIBODY

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Background and Aims:: Myasthenia Gravis (MG) and Lambert-Eaton Myasthenic syndrome (LEMS) are immune-mediated disorders of the neuromuscular junction. Clinical, electrophysiological and immunological overlap of these two conditions have been uncommonly reported. We report the unusual association of LEMS with muscle-specific kinase (MuSK) antibody associated MG.

Methods:: A 44-year-old lady who presented with exertional muscle pain and difficulty in standing from sitting position and lifting heavy weights of six years duration was evaluated with nerve conduction study (NCS), repetitive nerve stimulation (RNS) and enzyme linked immunosorbent assay (ELISA) for acetylcholine receptor (AChR) and MuSK antibodies.

Results:: Clinical features included normal blood pressure without orthostatic fall, bilateral ptosis, normally reacting pupils, limb-girdle weakness, waddling gait and exaggerated lumbar lordosis. Generalised areflexia was noted and stretch reflexes appeared after brief voluntary muscle contraction. There were no features of bulbar/ respiratory muscle weakness or dysautonomia. NCS showed reduced amplitude of evoked motor response (EMR) from the abductor pollicis brevis (APB), and post-exercise facilitation of 296.7%. RNS at 3Hz showed decrement 48.8%, while RNS at 20Hz showed an increment of 148%. MuSK antibodies were detected while AChR antibodies were absent. CT scanning of thorax and abdomen was normal. She was diagnosed to have LEMS-MG overlap and treated with steroids and azathioprine. At four months follow up, she reported 75% improvement in function.

Conclusions:: We report a rare patient with clinical and electrophysiological features of MG-LEMS overlap. The unique feature was presence of MuSK antibodies. MG, LEMS and overlap syndromes represent a continuum of disorders linked by antibodies to antigens in neuromuscular junction.
AN UNCOMMON CAUSE OF PARAPARESIS: THYROTOXIC HYPOKALEMIC PERIODIC PARALYSIS

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Background and Aims:: Thyrotoxic hypokalemic periodic paralysis (THPP) is an uncommon emergency mainly affecting Asian men. Stress, infections, high carbohydrate diet, steroids, physical activity are triggers. The classic triad for diagnosis is thyrotoxicosis, hypokalemia and paralysis. The typical presentation consists of symmetrical proximal muscle weakness (with legs more affected than arms, with extensor muscle more involved than flexors), promptly solved by the correction of hypokalemia.

Methods:: Case presentation A 56-year-old male from the Philippines presented to the emergency department with a sudden onset of weakness and pain of lower limb. He reported six months history of heart palpitations and hands tremors. Neurological examination revealed mild symmetrical paraparesis, hyperreflexia, fasciculations, hands tremors, without sensory or cranial nerve involvement. Systemic symptoms were fever and profuse sweating, along with new-onset atrial fibrillation. Magnetic resonance imaging of spinal cord and nerve conduction studies were normal and ruled out infections or inflammatory neuropathies. Laboratory data showed potassium 2,7 mmol/l (normal value 3,4 - 4,5), thyroid stimulating hormone < 0,005 mIU/L (normal value 0,270 - 4,200), thyroxine 65,3 ng/L (normal value 9,3 - 17,0), and triiodothyronine 16,0 ng/L (normal value 2,0 - 4,4), TSH receptor antibody 11,1 IU/L (normal value < 1,8) and anti thyroperoxidase > 600,0 kIU/L (normal value < 34,0).

Results:: He was treated with potassium supplementation, Propranolol, Methimazole and Propylthiouracil with favorable evolution.

Conclusions:: Thyroid function must be evaluated in differential diagnosis for acute paraparesis with normal electrophysiological and imaging studies. Management of THPP includes potassium supplementation, nonselective beta-blockers and achievement of euthyroid state.
TARGETED PHARMACOTHERAPY FOR TRAFFICKING DEFECTIVE CLC-1 MUTATIONS IN MYOTONIA CONGENITA

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Background and Aims:: A delayed muscle relaxation after a voluntary contraction is the main clinical feature of myotonia congenita (MC). MC is a skeletal muscle channelopathy caused by loss-of-function mutations in the ClC-1 chloride channel, which impair channel function or plasma membrane expression. To date, no direct activator of ClC-1 channel is known. A potential strategy may be to restore surface expression of trafficking-defective ClC-1 mutants by using pharmacological chaperones. Thus, we tested the ability of niflumic acid (NFA), a reversible inhibitor of ClC-1, to restore membrane expression of MC ClC-1 mutants (A531V, V947E, G411C).

Methods:: The HEK293 cells transfected with wild-type (WT) or MC ClC-1 channels, incubated in control conditions or in presence of 50 µM NFA, were used for patch-clamp recording, biotinylation assay, and confocal imaging.

Results:: Trafficking defect induced an absence (as for G411C) or marked reduction (as for A531V and V947E) of ClC-1 chloride currents. Incubation of transfected cells with NFA enhanced A531V and V947E chloride current density more than three-fold, thereby restoring WT-like currents. NFA incubation also improved V947E protein expression on the plasma membrane, as assessed by biotinylation assay. In contrast, NFA did not restore G411C chloride currents, suggesting lack of chaperone effect or G411C inability to conduct currents. The G411C channel surface expression was rescued by the proteasome inhibitor MG132 but no chloride current was recorded, indicating that G411C produces nonfunctional ClC-1 channels.

Conclusions:: NFA could be repurposed to MC patients carrying trafficking-defective ClC-1 channel mutations, designing a mutation-driven precision medicine in MC.
A NEW CYS1678TYR MUTATION RESPONSIBLE OF LGMD2B IDENTIFIED IN A FAMILY FROM SOUTHERN ITALY

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Background and Aims:: Mutations in the gene DYSF encoding dysferlin are responsible for dysferlinopathies. Dysferlin is mainly expressed in cardiac and skeletal muscle and appears to play an important role in the repair of the plasmalemma. Intra- and inter-family phenotypic variability has been reported in the literature for mutations in the DYSF gene. A new Cys1678Tyr mutation responsible of LGMD2B has been identified in a family from southern Italy.

Methods:: Genomic DNA was extracted from peripheral blood lymphocytes of all family’s affected and unaffected subjects using standard protocol. We developed a panel comprising 40 genes involved in LGMDs. The sequencing process was conducted on Ion Torrent PGM platform, annotation of variant calling by WANNOVAR. All the variations founded were confirmed by direct resequencing ABI PRISM 3130xl Genetic Analyzer.

Results:: Molecular analysis of three patients from a southern Italian family allowed the identification of a new G5036A mutation in the DYSF gene responsible for LGMD 2B. This mutation determining the replacement of a cysteine in position 1678 with a tyrosine predicted to be deleterious by PolyPhen and silico SIFT analysis. Moreover, Swiss model pipeline analysis showed that this mutation causes the breaking of a strong disulfide bridge with important consequences on the protein activity.

Conclusions:: The identification of new mutations responsible for LGMD2B and the study of several affected families will contribute to the identification of additional genetic, epigenetic, environmental factors responsible for the intra and inter-family variability reported in the literature. Furthermore, this will determine the development of new therapeutic targets and personalized medicine.
Background and Aims:: With the advent of new therapies, early diagnosis in spinal muscular atrophy (SMA) is essential. The aim of this study is to analyze the various components of the all too prevalent diagnostic delay.

Methods:: Patients with a confirmed molecular SMA diagnosis (types I, II, III) were included. We studied among other parameters age and first presenting sign, as well as interval between clinical onset and confirmed diagnosis. Telephone or face-to-face interviews were conducted by neuromuscular neurologists and supplemented when necessary with medical records' reviews.

Results:: Cohort included 112 patients. SMA I n=40, SMA II n=48, SMA III n=24. Mean age (months) at first reported sign was (X): SMA I 2.2±2.2, SMA II 9.7±4.1, SMA III 32.7±42.2. The first signs were noticed by parents 75 to 85% of the times in all three types. Time elapsed (in months) between the first sign and first medical consultation was on average less than a month for SMA I and II and 2.3 months for SMA III. Time elapsed between the first sign and confirmed diagnosis for SMA I: Me: 2 (IQR:1-4) (R:0-11); for SMA II: Me: 10 (IQR:16-25) (R:3-46) and for SMA III, Me: 31.5 (IQR:14.25-98.25) (R:4-288).

Conclusions:: There is significant diagnostic delay in SMA, shortest in type I and longest in type III and possibly related to several factors such as the severity of the disease, the healthcare system and the lack of treating physician's recognition of "tell-tale" signs.
Background and Aims:: The spinal muscular atrophy (SMA) landscape has changed over the last few years with the appearance of different therapeutic approaches. However, limited information is available about physicians' therapeutic decisions. The aim of this study is to assess how pediatric neurologists make decisions on treatment initiation, switch, and discontinuation in SMA applying principles of behavioral economics.

Methods:: The DECISIONS-SMA is a multicenter, non-interventional, cross-sectional, web-based study. Pediatric neurologists involved in the care of patients with SMA will be invited to participate in the study by the Spanish Society of Pediatric Neurology (SENEP). Participants will complete a survey on risk preferences and management of eleven simulated case-scenarios mimicking the current treatment landscape. Case scenarios will assess attitude, enablers and barriers to initiate, switch or withdraw treatments in patients with SMA types I-III. Motor, respiratory, and patient-centered outcomes (quality of life and activities of daily living) will be explored. Concomitant behavioral characteristics that could be associated with decision making will be assessed, including: therapeutic inertia, care-related regret, herding, and occupational burnout.

Results:: Recruitment will begin in May 2021 with a planned total sample of 50 pediatric neurologists throughout Spain.

Conclusions:: The study results are expected to enhance our understanding about decision making, therapeutic goals and expectations among pediatric neurologists caring patients with SMA.
BACKGROUND AND AIMs: Becker muscular dystrophy (BMD) is a dystrophinopathy due to in-frame mutations in the dystrophin gene determining a reduction of dystrophin. It is characterized by a wide clinical spectrum as to motor disability, progression and cardiac involvement. Standardized motor scales are commonly used to quantify motor impairment. Muscle magnetic resonance (mMRI) has become a non-invasive tool for diagnosis and follow-up, along with cardiac magnetic resonance (cMRI) to monitor cardiomyopathy. Here we present a two-years prospective evaluation of ten adult BMD patients, through standardized functional scales, mMRI and cardiological assessment.

METHODS: We recruited ten patients (aged 25-63; eight with a 45-x deletion, one 47-48, one 48), evaluated at baseline with the 6MWT, NSAA and W&GM scale, and then after one and two years. Muscle MRI was performed at baseline and then after two years. Each patient underwent cardiological assessment with echocardiogram, NT-pro-BNP measurement and in a subgroup of 5 patients, cMRI.

RESULTS: Three asymptomatic patients at baseline showed no disease progression, while the other patients presented a declining trend in motor functions measured by motor scales; notably the W&GM scale was stable overtime. Muscle MRI paralleled the clinical picture overtime. Cardiologic evaluation revealed pump impairment in the majority of patients and cMRI detected alterations in all the tested patients.

CONCLUSIONS: To date, longitudinal cohort studies evaluating BMD natural history are not available. Our study describes disease progression rate in adult BMD subjects affected by different forms of disease - from asymptomatic to moderate-severe impairment. Multiparametric studies on a larger cohort are needed to expand our understanding of disease progression towards trial readiness for BMD.
Background and Aims:: Glioblastoma can be histologically determined by the presence of neoplastic cells with astrocytic characteristics. Therefore, researchers become interested to improve the therapy for GBM either by novel nano delivery systems or by new therapeutics or by supplementing existing therapy.

Methods:: The study involves the fabrication of lomustine-loaded biodegradable nanofibres prepared by electrohydrodynamic (EHD) techniques which utilize electrostatic forces as the driving force to fabricate nano-range nanofibres. The prepared nanofibres formulation were characterized using surface morphology analysis techniques such as by AFM, SEM, TEM analysis, dug release, in-vitro and elution method and a HPLC assay were employed to characterize the in vitro and in vivo release behaviors of drug in Albino Wistar Rats bearing tumors from the electrospun nanofibres and also cytotoxicity of nanofibers was evaluated by MTT assay in U87 MG Brain tumor cell line.

Results:: In vivo results shows primary tumor resection decreased in treated with oral administered nanofibers, compared with the blank nanofibres, systemically administered drug, and the control group. Furthermore, better drug transport is achieved without interfering with the normal function of the brain. No inflammation reactions were observed in histological examination of the cerebral tissues.

Conclusions:: The experimental results show that the biodegradable nanofibres released high concentrations of drug with high drug loading and drug-releasing efficiency after oral formulation in the cerebral cavity of rats showing excellent biocompatibility. It also reveals that adopting drug-eluting nanofibres may result in sustained delivery of anti-tumor drug in the cerebral cavity in order to attain the enhanced therapeutic effect of Glioblastoma tumors treatment.
HOW LONG AND HOW FREQUENT FOLLOW-UP CARE SHOULD BE FOR LOWER-GRADE GLIOMAS? RETROSPECTIVE STUDY ON PATIENTS WITH LGGS AT NEUROLOGICAL INSTITUTE BESTA OF MILAN

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Background and Aims:: Glioma is the most common primary brain cancer in adults. Survival varies significantly by grade across glioma subtypes. The recent developments have led to the new term "lower-grade glioma" (LLG) to designate both grades II and III gliomas. These gliomas are best treated with a multidisciplinary team approach, including specialists from neurosurgery, radiology, pathology, radiation oncology, and neuro-oncology. In Italy, it is unclear how long follow-up care should last and whether the primary care sector is either willing or able to take this on. The aim is to determine pathways of follow-up care for LGGs and evaluate the professional attitude of doctors to prescribe to patients visits and exams after surgery.

Methods:: A retrospective study was performed on patients with LGGs who underwent surgery at tertiary care Neurological Institute Besta of Milan (FINCB) from 2012 to 2020. Data were collected through electronic medical records and inserted in an ad hoc developed database.

Results:: Three pathways have been identified: a common preliminary pathway (from the pre-operative visit to surgery) for all patients undergoing surgery for Gliomas II and III and two follow-up pathways (with or without second surgery).

Conclusions:: FINCB has developed care pathways that are sometimes personalized according to the doctor’s expertise and attitude to prescribe new examinations. Given the lack of guidelines on this issue, we can cautiously conclude that it is necessary to identify whether, in addition to standard care, personalized supportive care intervention.
PROLONGED REMISSION OF A PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA (PCNSL) AFTER CORTICOSTEROID THERAPY: A CASE OF VANISHED LYMPHOMA WITH LESIONS' SIDE CHANGE

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Background and Aims:: PCNSL is a rare form of non-Hodgkin lymphoma, accounts for 1 – 3% of adult intracranial neoplasm. Clinical and neuroimaging presentation may mimic progressive neurologic disorders. Corticosteroids (corts) can produce a quite variable apoptotic effect on PCNSL: partial volume reduction until its disappearance (vanishing lymphoma). Corts sensitivity of PCNSL is reported in 20 – 60% of cases. The aim of the study is to evaluate corts response in PCNSL patient in order to plan the timing of the biopsy.

Methods:: CASE REPORT A 73-year-old woman developed visual delusion and left hemiparesis. Neuroimaging showed multiple cerebral alterations in the right hemisphere. She underwent a needle biopsy after corts therapy, but the specimen was not diagnostic. She continued corts treatment with clinical improvement and complete regression of the lesion. There were not target for another biopsy for 18 months; then, she developed psychomotor retardation and right hemiparesis. TC scan showed multiple lesions in the left side of the brain. The patient underwent a new biopsy that showed B cell lymphoma.

Results:: Our patient with a history of vanished lymphoma showed a peculiar localization of lesions, first located in the right hemisphere, then in the left one. She had an extreme sensitivity to corts that caused the lesions to disappeared completely with a disease-free interval for about one year.

Conclusions:: PCNSL is a capricious tumor whose clinical course can be extremely rapid and, at other times, indolent, complicating the diagnostic choices, especially in organizing the brain biopsy and the use of corts.
TWO CASES OF PARANEOPlastic NEUROlogical SYNDROMES ASSOCIATED WITH non-Hodgkin LYMPHOMA.

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Background and Aims:: Lymphoma-associated paraneoplastic neurological syndromes (PNS) are a rare and ill-defined disorders. 

Methods:: We report two rare cases of PNS associated with non-Hodgkin lymphoma (NHL) from our single-center experience. Clinical, demographic data, treatments and outcomes are reported. 

Results:: A 72-years old female was admitted for subacute onset of gait instability and repeated falls. MRI showed cerebellar atrophy while 18F-FDG PET showed avid captation of laterocervical, mediastinal and para-aortic lymph nodes. Onconeural antibodies tested negative, type III oligoclonal bands were detected. Lymphnodes biopsies was consistent with small lymphocytic lymphoma. She was diagnosed with cerebellar paraneoplastic degeneration(PCD). She was treated with high-dose steroids and immunoglobulins without benefit. Her conditions rapidly worsened and she died of intercurrent infection. A 65-years old male was previously diagnosed with nodal marginal zone lymphoma and treated with rituximab-bendamustine. He was admitted for agitation, hallucinations, confusion and anterograde memory deficit followed by progressive tetraparesis with painful paresthesias in lower limbs. Brain and spinal MRI was negative. EMG showed sensory neuronopathy and lower motor neuron involvement. Onconeuronal antibodies tested negative. CT scans showed mild NHL progression. Paraneoplastic encephaloneuromyelitis was diagnosed and he was treated with high dose steroids, plasma-exchange and immunoglobulins with minimal improvement. The patient died of sepsis. 

Conclusions:: NHL-associated PNS are rare conditions that bear an unfavorable prognosis and they usually present in later stages of oncological disease. PCD is rare in NHL, while motor neuron involvement is peculiar. Our patients were seronegative for onconeural antibodies and had a poor response to immunotherapy. Negative onconeural testing should not mislead the diagnosis.
KI-67 EXPRESSION AS A PROGNOSTIC FACTOR OF GLIOMA IN INDONESIAN POPULATION

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Background and Aims:: Introduction: The most common neoplasms in the human brain is glioma that consisted of gial cells. The subjectivity in interpretation of glioma and difficulties to identify mitosis will affect the determination of tumor grade, therapy and prognosis of the patients. Immunostaining of Ki-67 represents the ability of tumor cells to proliferate and related to survival of the patient. Objective: The purpose of this study is to reveal the association of the Ki-67 expression and survival of glioma patients in Indonesia.

Methods:: Methods: Seventy eight sampels were obtained from formalin-fixed embedded parrafin (FFPE) samples in Dr. Sardjito General Hospital. Ki-67 labeling index (LI) was calculated as the percentage of labeled nuclei per 1000 cells using 40x objective lens in the same random area, evaluated by 2 independent observers. The expression of Ki67 and Overall Survival (OS) was statistically analyzed using Kaplan-Meier analysis.

Results:: Results: Based on univariate analysis, age ≥60 years, high-grade tumors, infratentorial gliomas, and Ki-67 LI ≥10% were associated with poorer overall survival. However, in multivariate analysis, only infratentorial tumors and Ki-67 LI ≥10% were statistically significant as independent prognostic indicators of gliomas.

Conclusions:: Conclusion. Ki-67 LI ≥10% is associated with shorter overall survival in Indonesian glioma patients.
PARAVERTEBRAL NEUROBLASTOMA WITH SPINAL CORD COMPRESSION AND BREAST METASTASIS IN A CHILD

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Background and Aims:: Spinal cord compression is a rare but serious complication of malignancy in the children. Neuroblastoma (NB) presented with spinal cord compression and breast metastasis is uncommon.

Methods:: We report here the first case of paravertebral NB in an adolescent girl with bilateral metastatic deposits in the breast.

Results:: A 13-year-old girl was admitted for acute weakness in the lower limbs and urinary retention. Neurological examination showed a flaccid paraparesis and thermo-painful anesthesia with sensory T8 level. General examination showed bilateral breast masses. A spinal MRI was performed, which revealed a large right paraspinal mass at the thoracic spine levels from T7 to T10. This lesion extended through multiple neural foramina causing severe spinal cord compression. The CT guided biopsy of the paraspinal lesion as well as the ultrasound-guided breast biopsy concluded to NB associated to N-Myc gene amplification. The child was referred to oncologist and combined chemotherapy was given.

Conclusions:: Up to 15% to 30% of pediatric malignant spinal cord compressions were due to NB. Management of NB involvement of the spinal canal requires prompt diagnosis and early treatment to relieve spinal cord compression because neurological manifestations of less than 4 weeks can generally have complete recovery, but longer period of symptoms without treatment often leads to long-lasting or even irreversible problems. Metastasis to the breast from an extramammary malignant neoplasm, including NB, is exceptional. Only three reported cases of high stage olfactory NB with unilateral metastasis to the breast have been previously described in the literature.
MULTIPLE CRANIAL NERVE PALSIES AS THE PRESENTING SYMPTOM OF DIFFUSE LARGE B CELL LYMPHOMA

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Background and Aims: Cranial neuropathies in Large B Cell Lymphoma (DLBL) is rare, but could occur at any stage of the disease. Third and seventh nerves are the most affected cranial nerves. Direct lymphoid infiltration and leptomeningeal spread are the main identified causes for this involvement. We report a patient presented with rapid onset bilateral third, left sided sixth and seventh cranial nerve palsies, whom later diagnosed with DLBL.

Methods: Case A 65-year-old patient with back pain for 3 months presented with insidious onset isolated right sided complete medical Oculomotor nerve palsy. His MRI brain and orbits were normal except an incidental finding of Faix meningioma (fig.1). 10 days later he again presented with rapidly progressed left sided third, sixth and upper motor seventh cranial nerve palsies. 3T-MRI brain and orbit with contrast only revealed mild enhancement in left sided third and seventh cranial nerves. (fig.2) His MRI spine done for back pain showed Para spinal soft tissue mass (fig.3) and biopsy done from the mass revealed the histological diagnosis of DLBL. Meanwhile his CSF had elevated protein with 8 lymphocytes and moderate number of atypical cells with large irregular nuclei.
Results: This patient's MRI evidence of possible meningeal deposits of Lymphoma with abnormal CSF may suggest leptomeningeal spread of lymphoma causing cranial neuropathies.
Conclusions: Cranial nerve involvement of DLBL is infrequent and can happen rarely in early stages of the disease. Isolated cranial nerve palsies must be evaluated thoroughly. Treatable neoplasms are one of the important differentials to be considered in the workup.
ACUTE UNILATERAL OCULOMOTOR NERVE PALSY REVEALING A PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA IN AN IMMUNOCOMPETENT PATIENT

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Background and Aims:: Primary central nervous system lymphoma (PCNSL) is a rare (5% of PCNS tumors) and aggressive extranodal non-Hodgkin lymphoma arising within the brain, eyes, leptomeninges, or spinal cord in the absence of systemic lymphoma at the time of diagnosis.

Methods:: A case report of an uncommon presentation of PCNSL to highlight its increasing incidence in immunocompetent patients.

Results:: A 63 years old woman with no medical history consulted for acute onset binocular diplopia. Neurological examination showed a partial palsy of the left extrinsic commun oculomotor nerve. Brain MRI showed a mesencephalo-thalamic hypersignal-lesion on T2 and diffusion with an intense enhancement after gadolinium administration and no restricted diffusion. There was no clinical or biological sign for systemic disease and the cytological and immunological study of the cerebro spinal fluid was normal. She received corticosteroids with total amelioration. A control imaging performed 01 month later has shown persistence of the lesion which was enhanced after gadolinium, hyper-perfused with a lipid peak and an increase in the choline/N-acetyl-aspartate ratio. A stereotaxic biopsy was performed showing a large B cell lymphoma. Bone marrow biopsy, ophthalmological examination and a thoraco-abdominal-pelvic CT were performed and were normal. Our patient received induction chemotherapy with high-dose methotrexate, followed by consolidative chemotherapy.

Conclusions:: The revelation of LPSNC by an oculomotor disorder is rare and it was reported in only 21 cases. It should be evoked in the immunocompetent subject, given both the increasing frequency and the absence of pathognomonic radiological sign.
DIFFERENTIAL DIAGNOSTIC DIFFICULTIES OF LYMPHOMA PRESENTING WITH NEUROLOGICAL SYMPTOMS

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Background and Aims:: Lymphoma of the central nervous system (CNS), both primary and secondary, represents a rare subset of non-Hodgkin lymphoma. Incidence in immunocompetent patients is approximately 51 cases per 10,000,000 per year.

Methods:: Neurological examination, laboratory tests including flow cytometric (FCM) immunophenotyping of cerebrospinal fluid (CSF), magnetic resonance tomography of the head (MRI), biopsy.

Results:: We present three different clinical cases of patients with lymphoma of nervous system. First case is of a 44-year-old male admitted to the emergency department with meningo radicular irritation syndrome. Patient was with history for peripheral facial nerve palsy and MRI showing extra axial tumor formation in the left cavernous sinus area (image 1). Biopsy was performed 3 months earlier showing partially hyalinized connective tissue. Examination of CSF showed lymphocytic pleocytosis, atypical ones in different phase of mitosis. FCM of CSF gave the diagnose T-lymphoblastic lymphoma. The second case is of 50-year-old female with complaints of weakness and decrease sensation in lower limbs, dysphagia and facial nerve palsy. MRI of the brain was without lesions (image 2). The patient was with suspicion for Guillain-Barre but CSF examination showed lymphocytic pleocytosis (47% atypical). FCM of it gave the diagnose B-lymphoblastic lymphoma. The third case is of a 63-year-old male with right hemiparesis and progressive cognitive impairment. Several CTs and MRIs of the brain was performed with diffuse lesions in both hemispheres (image 3). It was discussed ischemic stroke, tumor, CNS infectious disease. Examination of CSF and trepan biopsy of bone marrow were without pathological changes. Patient was diagnosed with diffuse large B-cell lymphoma after brain tissue biopsy.

Conclusions:: CNS lymphoma is a rare disease. FCM of CSF and brain biopsy could help to make the right diagnose.
ATYPICAL PRESENTATION OF MENINGIOMA WITH CAVERNOUS HEMANGIOMA: CASE REPORT

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Background and Aims:: The investigation of choice for meningioma diagnosis is MRI and it usually offers a high degree of reliability especially when the tumor has a typical location and appearance such as: iso-/hyointense to grey matter in T1 weighted imaging that shows homogeneous enhancement of contrast (T1 C + Gd) and iso-/hyointense to grey matter in T2 weighted imaging; other characteristic signs that help with the imaging diagnosis are the dural tail, the white matter buckling sign or the spoke-wheel appearance of the vessels. Atypical presentation such as inhomogeneous enhancement due to cystic degeneration or coexisting of the meningioma with other tumors is rare and can frequently lead to misdiagnosis.

Methods:: We present a 40-years old female patient diagnosed with a fibrous meningioma (World Health Organisation grade I) with alterations of the neurofibromatosis type 2 gene (NF2) and a cavernous hemangioma that showed an unusual perilesional swelling with higher density than the cerebrospinal fluid on MRI and signs of contrast of the peritumoral lesion at computer tomography angiography (CTA) more suggestive of a hemangioma.

Results:: Patient underwent surgery under the neuronavigational electrophysiological protocol. At 3-month follow-up MRI showed almost complete resection with restant tumor in the lateral wall of the SSS.

Conclusions:: The association between meningioma and cavernous hemangioma is extremely rare. There is little data on molecular alterations in such associations. Whether it affects treatment prognosis should be seen.
ASSOCIATION OF SMOKING WITH IDH1 MUTATION IN GLIOMA

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Background and Aims:: Mutation of the IDH1 gene plays an important role in gliomagenesis and in determining glioma prognosis. Previous studies had shown an association between smoking and IDH1 mutation in lung cancer. However, this association in glioma is unclear. This study aimed to find an association between smoking and IDH1 mutation in Glioma patients.

Methods:: Genomic DNA was extracted from fresh glioma tissues or from formalin-fixed paraffin-embedded (FFPE) samples. Mutation analysis was performed using Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) or DNA sequencing. Data regarding smoking was obtained from the medical record.

Results:: This study included 110 glioma patients. IDH1 mutations were found in 21 (19.1%) of the patients. As many as 30 patients (27.3%) had a history of smoking (current or former smokers). As many as 33.3 % of smokers had IDH1 mutations. This percentage was higher than in the non-smoking group (13.8%). This difference was statistically significant (p=0.02). Smoking was also associated with glioma grading. There was a higher proportion of high-grade glioma (WHO grade III and IV) in the smoking group compared to the non-smoking group (81.5% vs. 55.6% respectively, p=0.018).

Conclusions:: Smoking is associated with IDH1 mutations and grading in glioma patients.
NUMB CHIN SIGN: THINK OF THE OMINOUS!

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Background and Aims:: Numb chin sign (NCS) is defined as reduced or absent sensation in an area of the chin and lower lip within the distribution of the mental or inferior alveolar nerves. NCS may be the preliminary symptom of malignancy or recurrence/metastasis in patients with cancer. Therefore, the occurrence of NCS warrants careful examination and monitoring of such patients and we aim to highlight the same through this case.

Methods:: We describe a 19-year girl, without any comorbidities, who presented with intermittent fever, 5 kilograms weight loss since the past 2 months and sudden onset numbness of chin for 20 days. Apart from haematological and biochemical evaluation, appropriate imaging and biopsy were performed to arrive at the diagnosis.

Results:: Examination was non-revealing apart from a numb chin (A). Routine blood investigations and cerebrospinal fluid examination (including malignant cytology sent twice) were normal. Magnetic resonance imaging of her brain (with contrast) revealed enlargement, along with contrast enhancement of the left Meckel’s cave (B). Bone marrow biopsy revealed hypercellular marrow with sheets of medium sized atypical cells consistent with acute leukemia of B lymphoid origin (C). She was treated with chemotherapy for the same but unfortunately succumbed to the illness.

Conclusions:: Presentation with numb chin, especially in young individuals should raise alarm bells and lead to a thorough search for an underlying malignancy.
Background and Aims: Diffuse midline glioma’s (DMGs) include central nervous system tumors, containing a characteristic H3K27M mutation and found in the midline location of brain and spinal cord. To determine the clinical, pathological, radiological & surgical outcome, disease severity of DMG patients who have undergone surgery and to find better therapeutic options.

Methods: 29 diffuse midline glioma patients were recruited. Clinical, pathological, radiological & surgical outcomes were noted and correlated with survival.

Results: KI67% was compared between <18 and >18yrs age groups, it was found that KI67% was higher in <18yrs age group (24.92±13.66, p = 0.08) compared to >18yrs age group (16.47±10.19) and found to have trend towards significance and it was also found that KI67% was significantly low in the population with >6months disease duration (12.2±4.712mnths, p=0.012) compared to <6months disease duration population (21.58±12.79mnths). Survival duration was significantly high in patients with age >18years (232.06±265.75days; p=0.02) compared to <18years age (50.16±47.79days). The patients who were taken the radiation therapy found to show significantly higher survival rate (341.25±318.05 days, p=0.05) compared to those who were not taken (69.89±71.5). Patients who required shunt placement found to have significantly lower survival duration (43.6±30.35 days, p=0.02) compared to patients who did not require shunt placement (215.56±263.55 days). Patients with improved post op outcome (10.8±4.08, p = 0.002) were having significantly low level of KI67% compared to not improved cases (21.87±12.58) and KI67% was negatively correlated with survival duration (r=-0.40; p=0.0358).

Conclusions: Our study conclude that KI67% and H3K27M serves as the markers and are correlated with survival duration.
POEMS SYNDROME ASSOCIATED WITH INTRAMEDULLARY PLASMACYTOMA MIMICKING ATYPICAL CIDP

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Background and Aims:: POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, M protein, Skin changes) is a rare plasma cell disorder associated with sclerotic bone lesions and demyelinating neuropathy. It can present similar to CIDP (Chronic inflammatory demyelinating polyneuropathy), hence causing a diagnostic difficulty

Methods:: We present a case of 42-year-old gentleman with diabetes who presented with progressive limb weakness for 3 months causing him to be bed bound. He had bilateral symmetrical motor and sensory neuropathy with global areflexia, pedal oedema, skin pigmented and splenomegaly with liver parenchymal changes.

Results:: Nerve conduction study revealed sensory motor demyelinating neuropathy. CSF protein was high with no cellular reaction. These findings supported CIDP. Conventional treatments with immunoglobulin and plasmapheresis proved to be ineffective. MRI spine, sural nerve biopsy, bone marrow biopsy, CECT chest abdomen and viral screening were normal. His initial serum protein electrophoresis (SPE) was normal. The atypical nature of his demyelinating neuropathy lead to further investigations with radiology showing intramedullary infiltrating, lytic bony neoplasm in left pelvis which was biopsy proven to be an intramedullary plasmacytoma. Repeated SPE demonstrated abnormal monoclonal band confirming diagnosis of POEMS syndrome.

Conclusions:: Erroneous diagnosis of polyneuropathy due to CIDP in such cases could be costly. Prolonged treatment with IVIG and plasma exchange only is expensive and ineffective. Poor response to treatment and presence of other peripheral features should raise the possibility of other underlying causes such as paraproteinemia. Though POEMS syndrome is known to have osteosclerotic bone lesions plasmacytoma associated POEMS syndrome may cause lytic bone lesions.
CONTRIBUTION OF COMPARATIVE GENOMIC HYBRIDIZATION (CGH) TO THE CLASSIFICATION OF DIFFUSE GLIOMAS

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Background and Aims:: Diffuse gliomas are the most common primary malignant tumors of CNS in adults. These tumors are classified based on the recommendations WHO 2016 and cIMPACT-NOW. This classification results in an “integrated histo-molecular diagnosis” with better clinical correlation. In fact, it takes into account the results of genetic analyzes. The objective of our work is to discuss the contribution and limitations of CGH to classify diffuse gliomas and describe a cohort of patients with this tumor.

Methods:: It is a descriptive study of diffuse gliomas whose DNAs were sent to the cytogenetics service of the Lyon Hospices Civils for CGH. For each patient we collected age of tumor discovery, sex, tumor location and results of histological, immunohistochemical and genetic analyzes. In regards to CGH, we have tried to adapt this technique to DNA extracted from FFPE tissues.

Results:: We collected 16 patients. The age of discovery of the disease is on average 60 years. Tumor locations are variable. CGH’s technique has been validated in all cases. Based on the latest recommendations of WHO and cIMPACT-NOW, the gliomas were divided into 1 oligodendroglioma, 6 IDH mutant astrocytomas grade II or III, 3 IDHwt diffuse gliomas grade II or III and 6 glioblastomas.

Conclusions:: CGH is an efficient and in some cases essential tool to evaluate the prognosis and to adapt the treatment of gliomas. In view of this work, we wish to follow the evolution of our patients for a possible genotype prognosis correlation and to interpret all the anomalies observed in CGH.
INVOLVING PATIENTS AND CAREGIVERS IN THE PRODUCTION OF GUIDELINES FOR PALLIATIVE CARE IN PRIMARY BRAIN TUMOURS: IDENTIFICATION OF INTERVENTION PRIORITIES

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Background and Aims:: Involving patients and caregivers is an important component of clinical guideline development. The three main Italian scientific associations for neurology, neuro-oncology and palliative care (SIN-AINO-SICP) recently appointed a joint task force (TF) of clinicians and researchers to develop specific guidance on palliative care of people with primary brain tumours, following the GRADE approach. To identify clinical questions meaningful to the patients and caregivers, a qualitative approach was used.

Methods:: Based on the existing literature and on consensus, the TF identified nine intervention areas, whose relevance was apprised by patients (via personal semi-structured interviews) and bereaved caregivers (via focus groups, FGs) from five tertiary neuro-oncology centres. Participants were prompted to provide their personal disease-related experience, and were asked to elicit the areas that mostly impacted their own lives. Interviews and FGs were audio-recorded, transcribed and analysed using thematic analysis.

Results:: Twenty interviews and five FGs (28 caregivers) were completed between late 2020 and early 2021. Preliminary findings show that all the pre-specified areas were defined as important by participants. Most discussed topics were communication, organization and service satisfaction, cognitive and psychological issues, and advance care planning (ACP). Caregivers focused their discussions on the need for patient psychological support, difficulties experienced with symptoms control (e.g. epileptic seizures, behavioural changes), communication and organizational issues.

Conclusions:: Participation of Italian patients with brain tumours and family caregivers was high and information-rich. All of the nine guideline intervention areas were considered important, communication, care organization, symptom control and ACP being the most discussed.
MONITORING OF COGNITIVE FUNCTIONS AND QUALITY OF LIFE, IN GLOBLASTOMAS TREATED WITH REGORAFENIB

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Background and Aims:: Standard treatment for progression in glioblastomas is represented by nitrosureas and bevacizumab. Since January 2020, regorafenib has been added. An Italian randomized study suggested a potential advantage of regorafenib over standard therapy. However, the impact of regorafenib on cognitive functions is not known. The aim of this study is to evaluate the impact of regorafenib on the cognitive functioning and quality of life of adult with glioblastoma.

Methods:: Patients with early progression to MRI after radiotherapy and chemotherapy are included in the study. They are monitored every 3 months using a 30-minute neuropsychological battery of ad hoc tests as follows: long-term verbal memory (Hopkins Verbal Learning Test-Revised), executive functions (Controlled Word Association Test) and visual attention, ideomotor speed, spatial research (Trial Making Test). Quality of life is assessed using the European Organization Research Treatment Cancer (EORTC) quality of life questionnaires for brain tumors (C30, BN20). The timing of the assessment is before regorafenib (baseline), after three and six months of treatment.

Results:: Since February 2021, ten patients, six males and 4 females with an age range of 24-74, were eligible to enter the study and have started cognitive and quality of life monitoring. The study is ongoing.

Conclusions:: The expected results concern the trend of cognitive functioning and quality of life (improvement vs stability vs deterioration) and the identification of the types of cognitive functions most involved. Progression represents a critical issue for the study, as some of these patients could drop out during the monitoring phases.
THE ASSOCIATION BETWEEN IDH1 MUTATION AND MGMT PROMOTER METHYLATION IN INDONESIAN GLIOMA PATIENTS

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Background and Aims:: Gliomas are one of the most common brain tumors in adults. IDH mutation occurs in approximately 80% of all lower-grade glioma (LGG) and secondary GBMs. MGMT promoter methylation is an important marker to predict response to temozolomide chemotherapy. IDH1 mutation has been shown to be associated with MGMT promoter methylation. However, data about this from Indonesian glioma patients is very limited. Here we assessed the association between IDH1 mutation and MGMT promoter methylation status in Indonesian glioma patients.

Methods:: This was a retrospective study involving patients with glioma in Dr. Sardjito General Hospital and the affiliated hospitals. Genomic DNA was extracted from fresh glioma tissues or formalin-fixed paraffin-embedded (FFPE) samples. Mutation analysis was performed using Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) or DNA sequencing. MGMT promoter methylation status was identified using methylation-specific quantitative real-time PCR.

Results:: In total, 121 patients were included in this study. There were 29 patients with mutations in the IDH1 gene and 34 patients with MGMT promoter methylation. There was a higher proportion of MGMT methylation in the IDH1 mutant group than the IDH1 wild-type group (58.6% vs. 18.5%, p< 0.001).

Conclusions:: There was a significant association between IDH1 mutation and MGMT promoter methylation in Indonesian glioma patients.
ABDUCENS NERVE SCHWANNOMA: A CASE REPORT

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Background and Aims: Abducens schwannomas are rare tumors, representing less than 1% of all intracranial schwannomas in the literature. The tumor may be located within the cavernous sinus or more commonly at the prepontine region.

Methods: We reported a case of patient referred to the neurology department in Sahloul Hospital, Tunisia diagnosed with Abducens schwannomas;

Results: A 50-year-old woman presented with one month history of horizontal diplopia and headache. Right abducens nerve paresis was noted on neurologic examination. Facial sensation and corneal reflex were normal. The remainder of the physical examination was normal. Magnetic resonance imaging revealed a 6 x 5 mm sized heterogeneously enhancing mass in the right cerebellopontine angle. Although schwannoma was suggested, given the small size of the tumor, surgery was not indicated.

Conclusions: Intracranial schwannomas are benign, slow-growing tumors accounting for 6% to 8% of primary brain tumors. However, the majority has involved vestibular nerve and, less commonly, trigeminal nerve. Schwannomas of the cranial nerves involved with ocular motility are uncommon. Comprehensive radiographic evaluation together with the aid of advanced exquisite imaging technique can provide much more information on accurate diagnosis and microsurgical anatomy regarding the relationship of cranial nerves and microvasculature. Although MRI findings in the present case was considered consistent with schwannoma. In such cases, with no invasion of the cavernous sinus, radical tumor resection with preservation of the abducens nerve can be performed via a simple suboccipital retrosigmoid approach. Abducens schwannoma, although rare, should be taken into account for differential diagnosis of the cerebellopontine angle tumors.
CASE REPORT: GLIOSARCOMA IN PATIENT WITH SJOGREN SYNDROME

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Background and Aims: We describe a patient with Sjogren syndrome with rapidly progressive dementia due to gliosarcoma.

Methods: Female, 48 years old, presented with a memory dysfunction for 6 months and getting worse over time. The patient had complained about extreme fatigue, xerostomia, xerophthalmia, dysphonia, swallowing difficulty and diagnosed with Sjogren Syndrome for 3 years. She was then diagnosed with Rapid Progressive dementia and underwent MRI. The first MRI in September 2020 showed a hyperintense lesion in T2 and FLAIR along bilateral lateral periventricular, and contrast-enhanced diffuse nodules lesion in the left frontal lobe concluded as a demyelinating process. The second MRI in 2020 November 2020 showed a multiple solid-cystic lesion, with contrast enhancement on the solid part in cortical and subcortical of the bilateral frontal lobe, corpus callosum, and insulae. The lesions showed increased perfusion in CBV and CBF.

Results: Surgery was taken to resect the mass, and the pathology reveals the mass as gliosarcoma, WHO grade IV. Temozolomide 120 mg was given for 5 days and radiotherapy was given 8 times out of plan 33 times and was discontinued because of severe thrombocytopenia dan cardiomyopathy.

Conclusions: Gliosarcoma is a rare variant of a primary tumor of the central nervous system which very rarely shows rapid progressive dementia as an early clinical manifestation. In Sjogren’s syndrome, cognitive dysfunction can be also founded in some cases. This patient initially showed an MRI image that resembled a demyelinated lesion which was probably related to her Sjogren’s syndrome which was later found to be a malignancy.
A CASE OF STROKE AS THE FIRST PRESENTATION OF UNDERLYING PROSTATIC MALIGNANCY

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Background and Aims: Both ischemic and hemorrhagic stroke are well-recognized as complications of cancer and may be its initial manifestation. Pancreas, gallbladder, stomach, colon and gynaecological malignancies have all been associated with stroke.

Methods: We present ischemic stroke as the initial manifestation of prostatic cancer.

Results: A 62-year-old male with no medical history was admitted to our department after sudden onset left hemiplegia. Initial examination showed dysarthria, left homonymous hemianopia, left hemiplegia and purpuric skin lesions on his trunk and extremities. MRI brain demonstrated infract in the territory of the right middle cerebral artery. The etiological investigations: a cardiac ultrasound, 24hours ECG Holter and CT angiography of supra-aortic trunks showed no etiology. Laboratory investigations were suggestive of disseminated intravascular coagulation. CT abdomen and pelvis demonstrated enlarged heterogeneous prostate. Prostate specific antigen was raised more than 1000000ng/ml. A bone radionuclide imaging showed extensive metastasis. Prostate biopsy revealed an adenocarcinoma. The patient presented severe anemia and thrombopenia with hemorrhagic complication. He was initially treated by blood transfusion, then he was referred to oncology departement to start hormonotherapy.

Conclusions: Physicians should consider an underlying cancer as a potential explanation for a cryptogenic ischemic stroke particularly if the stroke is associated with abnormal blood studies. Authors recommended that etiological investigations should include a thoracic, abdominal and pelvic CT-Scan. Many mechanisms may explain the relation between ischemic stroke and active cancer as the disseminated intravascular coagulation, non-bacterial thrombotic endocarditis, secondary infections or direct tumor invasion. Early detection of underlying malignancy remains an essential driver of improved prognosis.
CORRELATION OF NEUTROPHILS LYMPHOCYTE RATIO WITH FUNCTIONAL OUTCOME IN INTRACRANIAL TUMOUR

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**Background and Aims:** Background and aims: Intracranial tumors are one of the causes of high rates of morbidity and mortality in neurology patients. Currently required laboratory markers can be used and correlated with functional outcome. Neutrophils Lymphocyte Ratio (NLR) is an inflammation marker used as a parameter of prognosis in various tumors. Increased of NLR have been known before its significant relationship with immediate survival rate in intracranial tumour by functional outcome. This study want to determine the correlation of neutrophils lymphocyte ratio with functional outcome in intracranial tumour.

**Methods:** This study uses a cross-sectional design. Sampling was conducted at Adam Malik General Hospital Medan. Samples were taken as many as 40 subjects consecutively. Blood laboratory and functional outcome were checked on days 1 and day 12. Data analysis used the spearman test and Pearson correlation test.

**Results:** Results of the study: Demographic characteristics of the study subjects were an average age 40-59 years, females 60% and 40% males, high school education level, housewife occupation. As many as 52.5% were primary brain tumors and 47.5% were metastatic brain tumors. There was significant relationship between NLR with NANO score in intracranial tumour for day 1 (p=0.001, r=0.646) and day 12 (p=0.001, r=0.656). There was significant relationship between NLR with KPS in intracranial tumour for day 1 (p=0.001, r=-0.617) and day 12 (p=0.003, r=-0.451).

**Conclusions:** Conclusion: There was significant relationship between NLR with functional outcome in intracranial tumour by NANO score and KPS.
COGNITIVE DEFICITS IN CHILDREN WITH BRAIN TUMOURS: A PROJECT TO CREATE A SOFTWARE FOR COGNITIVE TRAINING.

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Background and Aims:: Brain tumors are the main cause of cancer-related death in children. These tumors and related treatments, in particular radiotherapy and high dose chemotherapy, are often associated with cognitive deficits that can cause mood and behavioral impairments. The aim of this study was to characterize cognitive impairments in children with brain tumors with the aim of creating a specific software for cognitive training to improve life expectancy and quality.

Methods:: The project had 3 phases: 1) defining the clinical and neuropsychological characteristics of children with brain tumors, 2) performing two systematic reviews on types of cognitive deficits and types of electronic devices available for cognitive rehabilitation 3) designing a software for cognitive training.

Results:: Between 2010 and 2020, 911 children with brain tumors were diagnosed by the Bambino Gesù Children's Hospital. Of these, 164 children (94 males; mean age 89±52 months, range 4-211), were consecutively enrolled by the emergency room. At a mean follow-up of 42±26 months (range 0-135) 12 patients had remitted, 36 were stable, 70 progressed, 44 died, and 2 were lost at follow-up. The histological diagnoses of the most frequent tumors were low-grade glioma (n=55), medulloblastoma (n=31), and ependymoma (n=16). In a preliminary evaluation of 9 children with medulloblastoma the general quotient score at diagnosis with the Griffiths Developmental Scale was 89± 16 (range 52-102).

Conclusions:: The identification and characterization of cognitive impairment over time are essential to define a specific technology for training (i.e. gaming app).
THE CORRELATION BETWEEN BRAIN TUMOR LOCATION AND ONSET OF NEUROOPHTHALMIC SYMPTOMS IN BRAIN TUMOR PATIENTS IN ADAM MALIK GENERAL HOSPITAL MEDAN

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Background and Aims:: Brain tumor is one of the tenth leading cause of death. Brain tumor can cause visual impairment by affecting the visual pathway. Important predictors for visual impairment are the tumor location (supratentorial or infratentorial) and elevated intracranial pressure. Patients with brain tumor often meet their ophthalmologist first. The signs and symptoms of neuroophthalmic can be one of suspicion to diagnose brain tumor. This study want to determine the correlation between brain tumor location and onset of neuroophthalmic symptoms in brain tumor.

Methods:: This study used a cross sectional design. Sampling was conducted at Ruang Rawat Inap Terpadu (Rindu) H. Adam Malik General Hospital Medan. Samples were taken as many as 30 subjects consecutively. Neurological examination and neuroophthalamic examination was performed in patients. Data analysis used the contingency coefficient test.

Results:: Demographic characteristics of the study subjects were in age >50-60 years, females>males, high school education level, housewife occupation. As many as 83,3% were primary brain tumors and 16,7% were secondary brain tumors. As many as 76,7% were located in supratentorial, 66,7% with onset ≥4,5 months and the most common neuroophthalmic symptoms was secondary headache due to raised intracranial pressure as many as 83,3%. There was significant relationship between brain tumor location with onset of neuroophthalmic symptoms in brain tumor (p=0,003).

Conclusions:: There was significant relationship between brain tumor location and onset of neuroophthalmic symptoms in brain tumor.
Background and Aims:: Paraneoplastic syndromes are rare, heterogeneous and might make the diagnosis of the underlying tumor. Although most clinical presentations are well described, some are atypical. Our aim is to establish a correlation between paraneoplastic neurological syndromes and the corresponding antibody, in a Tunisian series in comparison with the findings of the literature.

Methods:: Retrospective-descriptive study including patients with a confirmed diagnosis of a neurological paraneoplastic syndrome according to the Graus 2004 criteria. Epidemiology, clinical features and evolution were precised.


Conclusions:: Our study illustrates that the clinical spectrum of some onconeural antibodies exceeds the classical paraneoplastic syndromes (ex: anti-YO). In addition, positivity to more than one antibody is not exceptional. Some clinical presentations are unusual: multifocal presentation, Miller Fisher syndrome, multiple cranial nerve palsy. Screening for onconeural antibodies in these cases is mandatory if preliminary results are inconclusive. Diagnostic criteria might need to be updated and well established guidelines on the management of paraneoplastic syndromes are needed.
ATYPICAL INTRACRANIAL EXTRAMEDULLARY HEMATOPOIESIS AS A RARE COMPLICATION OF CHRONIC MYELOMONOCYTIC LEUKEMIA

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Background and Aims:: Extramedullary hematopoiesis (EH) in adults is rare and generally considered a compensatory mechanism in patients with chronic anemia and can occur in the course of myelodysplastic diseases. Cerebro-meningeal localization of EH is unusual and when it is present it is usually in the form of intracranial masses and it can course with neurological focus and epileptic seizures.

Methods:: We describe an unusual cerebro-meningeal EH case with history of chronic myelomonocytic leukemia and myelofibrosis criteria.

Results:: Male-67-years-old treated by idarubicina and citarabina 3 weeks ago, who presented an acute self-limited episode of disorientation with motor dysphasia and hypersalivation. The electroencephalogram showed no epileptic activity. Laboratory analysis showed pancytopenia (hemoglobin 8 g/dL, leukocytes 7880/µL, platelets 9000/µL) and mild hypertransaminasemia as unique remarkable findings. The brain magnetic-resonance (MRI) showed T1-hyperdensity and pachymeningeal enhancement with some nodulations; T2-hyperdensity was also seen at the supraorbital and left tempo-occipital sulcal level; the findings suggested extramedullary hematopoiesis at the meningeal level, with mild sulcal subarachnoid hemorrhage at the tempo-occipital level. Lumbar puncture could not be performed due to persistent thrombopenia. The control brain-MRI performed 2 weeks later showed partial resolution of lesions despite no specific treatment.

Conclusions:: EH is due to abnormal location of myeloid tissue in other organs than bone marrow. It is uncommon the cerebro-meningeal localization of EH secondary to chronic myelofibrosis. We describe a rare presentation with infiltrative pachymeningeal involvement and nodulations. Clinical evolution and succesives MRI can be useful to define the etiology in cases without possibility of pathological study.
THE INCIDENCE OF CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY AND COGNITIVE IMPAIRMENT IN PATIENTS WITH GASTROINTESTINAL TRACT CANCER

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Background and Aims:: While there are many anti-cancer drugs used with widely varying mechanisms of action, there appear to be a common set of symptoms induced by many of these agents which include fatigue, cognitive dysfunction, and peripheral neuropathy. Indeed, these symptoms can be so severe that physicians may be forced to deviate from the optimal treatment strategy for a patient, which can directly influence survival. This research aimed to determine the incidence of chemotherapy induced peripheral neuropathy and cognitive impairment in patients with gastrointestinal tract cancer.

Methods:: This prospective descriptive study conducted on 100 patients with gastrointestinal tract cancer randomly selected, based on the including criteria. We used a demographic form, modified Total Neuropathy Score (mTNS), and Functional Assessment of Cancer Therapy Cognitive (FACT-Cog3) questionnaire for data collection.

Results:: The mean age of patients was 58.59 ±10.13 years .The majority of them were male (70%), with gastric cancer (36%).In this study 63% of patients had chemotherapy induced peripheral neuropathy and 80% of them had chemotherapy induced cognitive impairment. The results of chi-square test showed peripheral neuropathy and cognitive impairment were significantly associated with the type of chemotherapy agents used. Unlike peripheral neuropathy, cognitive impairment had a statistically significant relationship with patients' gender.

Conclusions:: The findings of the present study indicate a high incidence of chemotherapy induced peripheral neuropathy and cognitive impairment among cancer patients treated with cytotoxic drugs. The type of chemotherapy drugs can also be used as predictors of peripheral neuropathy and cognitive impairment.
THE INFLUENCE OF POSTOPERATIVE INFECTIONS ON THE SURVIVAL OF GLIOMA PATIENTS

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Background and Aims:: Glioblastoma remains the most common and lethal brain tumor in adults with a poor prognosis. Thinking about immunological influences, the question if postoperative infections have any efforts on survival arises consistently. Of our knowledge, this is the first study to evaluate a large group of glioma patients with postoperative infections, itemized by intracranial, extracranial and systemic infection.

Methods:: We analyzed retrospectively 267 patients with glioma for any infection over 2 months after brain surgery and identified WHO-grade, age, treatment and survival times from 2008 to 2013 with follow-up until 2016. We classified into intracerebral, extracerebral and systemic infections.

Results:: We identified 87 patients with infections over 2 months after brain surgery and 180 patients without. Age and WHO-grading were comparable in both groups. Patients with infections had shorter median survival than without (19.1 vs. 41.1 months, \(p=0.022\)). Patients with glioblastoma and infection had a shorter median survival time than patients without (12.9 vs. 16.4 months, \(p=0.017\)). Itemized by the location of the infection there was no statistically significant difference between the median survival of the non-infectious and the intracranial infection group (16.4 vs. 17.4 months, \(p=0.349\)). Patients with extracranial or systemic infection had a much lower life expectancy (1.4 and 1.8 months).

Conclusions:: There was no survival advantage for patients having suffered a postoperative infection, but the location of the infection made a vast difference in survival time. Immunological mechanisms may play a role in future local therapeutic strategies, but have no positive effects, even sometimes negative, in normal patient treatment postoperatively.
AN UNUSUAL CASE OF RELAPSING LONGITUDINALLY EXTENSIVE TRANSVERSE MYELITIS

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Background and Aims:: Etiologies of longitudinally extensive transverse myelitis (LETM) include demyelination, granulomas and infections. We describe an uncommon cause of LETM with a relapsing course.

Methods:: The clinical and imaging profile and laboratory investigations of a 17-year-old male were reviewed.

Results:: The patient developed intermittent low-grade fever, sub-acute paraparesis and urinary retention. Spine MRI showed LETM from dorsal cord to conus, and leptomeningeal enhancement. Cerebrospinal fluid (CSF) showed polymorphonuclear pleocytosis (180 cells), elevated protein (115 mg%), and reduced glucose (17 mg%). He was empirically treated with anti-tubercular therapy (ATT) and steroids. He recovered completely over five months and steroids were stopped at seventh month. At 11th month, he developed acute progressive paraplegia, sensory level at T4 and double incontinence. ATT was continued and steroids were re-initiated. At 18th month, weakness progressed to involve upper limbs and sensory level ascended to C7. At 22nd month, he developed holocranial headache, vomiting, diplopia, ptosis, nystagmus and tongue fasciculations. At 24th month, he developed hydrocephalic attacks and underwent ventriculo-peritoneal shunting. At 25th month, he developed respiratory distress and cyanosis necessitating mechanical ventilation. MRI showed appearance of new enhancing lesions in anterior corpus callosum, periaqueductal region, brainstem and bilateral dentate nucleus. Serial CSF analysis showed persisting pleocytosis and elevated protein. Evaluation for vasculitis, sarcoidosis, neuromyelitis optica and tuberculosis were negative. Bone marrow study was normal. Vario-guided biopsy of dentate lesion showed diffuse large B-cell lymphoma.

Conclusions:: Lymphoma of spinal cord is rare. Protracted course in this patient with ‘relapses’ could be attributed to modification of disease course by steroid therapy.
GARCIN SYNDROME: A RARE MANIFESTATION OF NASOPHARYNGEAL CARCINOMA

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Background and Aims:: This is a case of a 38-year-old male with chronic ear pain, tinnitus, hearing loss, and effusion. The pain progressed with sudden multiple ipsilateral craniopathies. He was diagnosed with nasopharyngeal carcinoma as the primary cause of the Garcin syndrome. Literature on nasopharyngeal carcinoma presenting as Garcin Syndrome is very limited. Treatment and prognosis depend on the underlying pathology. Surgical option for nasopharyngeal carcinoma is usually limited to biopsy. Mainstay of treatment is combined chemotherapy and radiotherapy. Prognosis of nasopharyngeal carcinoma depends on the stage during diagnosis and the histology of the tumor. Our patient was given combined chemotherapy with cisplatin, 5-Fluorouracil and radiotherapy. Recommendations on appropriate management and prognosis is limited due to scant literature on the case.

Methods:: Case Report

Results:: Multiple cranial palsies can have many etiologies. A systematic approach to the case beginning with an exhaustive history taking and thorough physical examination complemented with radiologic workups is essential to a correct diagnosis and management. Extensive knowledge of the symptomatology and course of disease entities can help rule out intra-cranial and infectious pathologies and narrow our differential diagnoses. CT scan, MRI, and angiogram studies eliminated the vascular causes. Our radiologic work ups showed a mass lesion in the nasopharyngeal area with extension to the cranium and multiple cervical lymphadenopathies. Biopsy of the mass revealed nasopharyngeal carcinoma.

Conclusions:: Garcin syndrome is a rare cause of multiple cranial palsies. Garcin syndrome secondary to a nasopharyngeal carcinoma is even rarer. The appropriate management and prognosis of this case depends on the underlying pathology.
Background and Aims:: Cerebral venous thrombosis is a rare disease in children, but is one of the most serious complications of leukemia acute infantile lymphoblastic. We report the case of a child with acute childhood lymphoblastic leukemia, treated with L-asparaginase, who developed cerebral venous thrombosis.

Methods:: 12-year-old child with acute lymphoblastic leukemia, having received in the induction phase: methotrexate, purinol, endoxan, aracytine, and lastly asparaginase combined with corticosteroids. Three weeks later, the child presented with generalized serial tonic-clonic seizures. Examination: four-limb pyramidal syndrome predominant on the left. Brain MRI: bilateral frontal hemorrhagic infarction with thrombosis of the superior sagittal sinus (fig1) The child was put on keppra without anticoagulant, the child no longer had epileptic seizures.
Results: In acute lymphoblastic leukemia, the onset of thrombosis is due to the combination of different risk factors: the disease itself, the therapeutic attitude, the infections. This is the case of this child with this disease, treated with several molecules including L-asparaginase combined with corticosteroid therapy. L-asparaginase induces a state of hypercoagulability. Systematic and regular monitoring of fibrinogen and anti-thrombin III levels is therefore recommended. The administration of low molecular weight heparin followed by a relay with anti-vitamin K (3 to 6 months) is the recommended treatment.

Conclusions: The use of L-asparaginase requires careful clinical and laboratory monitoring. Cerebral thrombosis should be raised in the slightest doubt, requiring the temporary discontinuation of this drug, associated with specific management of the thrombosis, as well as a substitution on a case-by-case basis.
LANGERHANS CELL HISTIOCYTOSIS: CASE REPORT

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Background and Aims:: Langerhans Cell Histiocytosis (LCH), is characterized by expansive and erosive accumulations of Langerhans cells, which can occur in single or multiple tissues. The disease is rare, identified in approximately 0.5 per 100,000 children up to 2 years of age, shows a diverse clinical presentation, pathological commitment, and outcomes. Those factors make diagnosis and treatment difficult in LCH.

Methods:: We describe a case of Histiocytosis X in a male patient, aged 1 year and 6 months, with normal weight, height, and neuropsychomotor development for his age, who presented a tumor in the right temporal region and erythematous-squamous skin lesions with yellowish color on the scalp and trunk since his four months of age.

Results:: First, cranial Computed Tomography (CT) and temporal lesion biopsy were requested. The cranial CT revealed intense osteoclastic activity. Histopathological examination suggested LCH, confirmed by an Immunohistochemistry test that demonstrated CD1a-positive and S100-positive. To investigate systemic LCH, chest, abdomen, pelvis, and myelogram radiographs were requested, all without visible alterations. In addition, the patient's whole-body bone scintigraphy was requested, which identified multiple osteogenic reactions. The research proceeded with bone marrow biopsy, which showed infiltration by LCH, concluding the diagnosis of multisystem LCH. The patient had a favorable evolution to corticosteroid therapy associated with chemotherapy and has been monitored annually for recurrence research, the segment is maintained indefinitely.

Conclusions:: The case reported is notorious since its initial symptoms were discrete, with a single temporal tumor and skin lesions. This patients' LCH diagnosis occurred early, however, late diagnosis is common.
A CASE REPORT OF A BRAIN METASTATIC THYROID FOLLICULAR CARCINOMA SIMULATING A MENINGIOMA

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Background and Aims:: Follicular thyroid carcinomas present intracranial metastases in about 1% of cases, usually consisting of intraparenchymal lesions. In less than 10% of cases, these lesions can be exclusively dural, being able to mimic meningiomas on imaging exams. The prognosis for thyroid carcinomas with distant metastases is poor, especially when the affected site is the brain, with a mean survival of less than one year. Our aim is to report a simulated meningioma by a brain metastatic thyroid follicular carcinoma.

Methods:: Case report of a 37-year-old woman presenting with a 6-month severe headache complaint and progressive bulging of the skullcap that sought medical assistance at our service.

Results:: Cranial MRI revealed an expansive intra and extracranial extra-axial mass in the left frontoparietal area that was causing a severe midline deviation. The lesion was isointense on T1, slightly hyperintense on T2, exhibited homogeneous enhancement post gadolinium administration, and a minimum halo of edema around the tumor on FLAIR, suggestive of meningioma. She underwent intracranial tumor exeresis and received hospital discharge 5 days after the procedure in good general condition, without neurological deficit. Pathological analysis and immunohistochemistry reported calvarial metastatic thyroid carcinoma of follicular pattern. The patient was submitted to thyroidectomy and radioiodine therapy about 1 month later. After 8 months, she underwent cranioplasty, without intercurrence. At the moment the patient is being followed-up by the oncology team.

Conclusions:: Considering that the metastatic follicular subtype of thyroid carcinomas tends to be more aggressive, our patient had an outstanding outcome, with a successful surgical resection therapy to date.
VISION LOSS RELATED TO COVID-19 INFECTION: A CASE SERIES OF ATYPICAL OPTIC NEURITIS

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Background and Aims:: The Covid-19 outbreak, which was declared a global pandemic, has affected large human populations in many countries since March 2020. Although SARS-CoV-2 is a respiratory infection agent, various neurological syndromes, ranging from mild to severe, that may be associated with COVID-19 have been reported. Acute onset vision loss, optic neuritis (ON), cranial neuropathies, and Miller Fisher syndrome have been reported as covid-19-associated neuroophthalmological diseases. Objectives: In this case series, we aim to describe the clinical features of ON associated with COVID-19.

Methods:: We described the clinical laboratory and MR findings of our 3 patients who were diagnosed with COVID-19-associated ON after their application to our clinic.

Results:: Case 1: 18-year-old female patient presented with severe vision loss in the left eye. Examination showed visual acuity of finger movement from 40 cm and a left afferent pupillary defect with central scotoma. SARS-CoV-2 realtime polymerase chain reaction (RT-PCR) analysis of nasopharyngeal exudate and immunological testing was positive for IgM, suspicious for a possible active infection. Orbital magnetic resonance imaging (MRI) confirmed a left-sided optic nerve lesion on T2 weighted images. She was treated with IVMP treatment. Case 2: 56-year-old patient presented with blurred vision 1 month ago, he was diagnosed with COVID-19 and was treated with favipiravir. Visual acuity was 20/20 in the right eye and hand motions in the left eye. Cranial and orbital MRI were normal, patient was treated with IVMP. Case 3: 23-year-old patient presented with blurred vision in her left eye. Lymphopenia and SARS-CoV-2 PCR analysis of nasopharyngeal exudate were positive. Contrast-enhanced cranial and orbital MRI were normal, patient was treated with IVMP for 5 days.

Conclusions:: These 3 cases suggest that Covid-19 plays a role in the development of ON. The responsible mechanism may not be related to the direct infectious effect of the virus but rather a trigger role in autoimmune processes. Further studies are warranted.
CASE SERIES ABOUT DISJUNCTIVE NYSTAGMUS

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Background and Aims:: The mechanism and neural structures responsible for the disjunctive (disconjugate) nystagmus especially for divergence remain to be elucidated.

Methods:: We describe two patients with divergence nystagmus in association with lesions involving the dorsal pons and midline cerebellum.

Results:: Case 1. A 27-year-old woman was consulted for neuro-otologic evaluation three days after resection of cerebellar pilocytic astrocytoma mostly occupying the middle portion of the midline cerebellum around the fourth ventricle. Neurologic examination showed spontaneous divergence nystagmus during visual fixation, gaze-evoked nystagmus (GEN) during lateral gazes, more to the left, and limitation of abduction in the left eye. Convergence was intact. Video-oculography (VOG), seven days after the surgery, documented divergence nystagmus during visual fixation. Case 2. An 18-year-old woman visited the emergency department with acute dizziness for two days probably due to a large cavernoma involving the right cerebellum and pons. She additionally developed diplopia right after the visit. Examination showed right esotropia with limited abduction of the right eye along with rightward gaze palsy. She also showed spontaneous nystagmus beating outward in each eye and conjugate upbeat nystagmus with a clockwise component in the right eye and counterclockwise component in the left eye. After the emergent operation due to intracranial hypertension, the pathologic finding was consistent with cavernous hemangioma. Three days after the surgery, follow-up examination with VOG showed a resolution of the divergence nystagmus along with improved headache, dizziness, and nausea.

Conclusions:: Divergence nystagmus supports an active neural innervation for divergence, rather than passive relaxation after convergence.
Background and Aims:: Idiopathic intracranial hypertension (IIH) can cause disabling and permanent vision loss if it is not diagnosed and managed early. These findings are applicable only once the secondary causes of raised ICP are ruled out. Here we describe a patient of raised ICP secondary to severe iron deficiency anaemia causing vision loss.

Methods:: A 28 year old female presented to us with 6 months history of progressive holocranial headaches, associated with progressive bilateral loss of vision from 3 months. She had bilateral grade V papilledema and a visual acuity of counting finger (CF) till 1 meter in the left eye and 6/36 in the right eye (Fig.). The visual fields showed a generalised constriction of visual fields sparing a central island of vision (Fig.). Her Magnetic resonance imaging (MRI) of brain with venogram showed signs of raised ICP (Fig). Her CSF pressure was elevated > 400cms of water. She also had severe anaemia haemoglobin 6.8 g/dL with a low S.Ferritin levels of 15ng/mL. She was transfused 2 units of packed red blood cells (PRBCs). After 2 days of transfusion she noticed improvement in her visual fields.

Results:: She was discharged on oral haematinics, Acetazolamide 1000mg/dL and Topiramate 50 mg/day. A month after therapy her haemoglobin had increased to 8.8 g/dL, visual fields had cleared up (fig.) and visual acuity recovered to 6/6 in the right eye and 6/9 in the left eye.

Conclusions:: The diagnosis of IIH merits ruling out secondary treatable causes which might obviate surgery.
THE SPECTRUM OF OPTIC PERINEURITIS- A CASE SERIES

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Background and Aims:: Optic perineuritis (OPN) is an uncommon “inflammatory disorder” involving the optic nerve sheath. The term might be figuratively similar to Optic Neuritis (ON) which is an inflammation of optic nerves (and not the optic nerve sheath). We aim to describe the important clinical and radiological findings in patients with OPN.

Methods:: Where association of ON with demyelinating syndromes (Multiple sclerosis/ Neuromyelitis optica) is well known; OPN commonly presents with a background of Orbital inflammatory syndromes. The involvement of other orbital structures can be an important clue while diagnosing OPN. Neuroimaging usually clinches the diagnosis.

Results:: We provide a series of seventeen patients with varied causes of OPN. Clinical presentation, neuro-ophthalmological hallmarks and prognosis of patients with OPN need to be kept in mind while considering the prognosis.

Conclusions:: OPN is a comparatively rare localized form of orbital inflammatory diseases. It needs to be differentiated from ON because of different therapeutic and prognostic implications. The involvement of other ocular/orbital structures can be an important clue while diagnosing OPN. Secondary causes of OPN should always be borne in mind while investigating these patients.
WALL - EYED MONOCULAR INTERNUCLEAR OPHTHALMOPLEgia (WEMINO): CASE REPORT

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Background and Aims:: Internuclear Ophthalmoplegia (INO) is a disorder of ocular motility caused by the damage to the Medial Longitudinal Fasciculus (MLF), which allows coordinated eye movements towards a horizontal direction. Wall-Eyed Monocular Internuclear Ophthalmoplegia (WEMINO) is an uncommon clinical presentation of INO that associates ipsilateral exotropia; the underlying pathophysiology of the syndrome is not yet fully understood.

Methods:: Case report of a patient with WEMINO due to pontine stroke.

Results:: A 73 year old man with previous medical history of hypercholesterolemia, diabetes mellitus and ischemic cardiomyopathy, smoker of 20 cigarettes per day and under treatment with acetylsalicylic acid, metformin and rosuvastatin, presented to the ER referring acute onset diplopia and vertigo. Initial neurological examination showed exotropia of the right eye, adduction paresis of the right eye, abducting nystagmus of the left eye, upbeat bilateral nystagmus and paresis of convergence of the right eye (video-filmatino available). Brain Magnetic Resonance revealed acute ischemic infarction in the right upper paramedian pontine tegmentum adjacent to the 4th ventricle, in the area of MLF. Basilar artery showed mild atheromatosis. The patient was diagnosed with Wall-Eyed Monocular Internuclear Ophthalmoplegia (WEMINO), and treated accordingly. Three months later the diplopia and eye deviation had disappeared completely.

Conclusions:: The case we present depicts a very uncommon clinical presentation of INO. The precise mechanisms underlying ipsilateral exotropia are not yet fully understood, but the few clinical reports suggest WEMINO is caused by damage confined to the MLF. Clinicians must be aware of this disorder in order to promptly identify and treat it.
ATYPICAL NON-PARANEOPLASTIC AUTOIMMUNE RETINOPATHY WITH ANTI-RECOVERIN ANTIBODIES: A CASE REPORT

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Background and Aims:: Autoimmune retinopathy (AIR) is caused by antiretinal antibodies damaging the retinal tissue, classified as paraneoplastic or non-paraneoplastic. Non-paraneoplastic AIR usually presents as a rapidly progressive and often asymmetrical visual loss with an unfavorable visual prognosis. Only a few cases of non-paraneoplastic AIR associated with anti-recoverin antibodies have been described in literature.

Methods:: We describe an atypical case of non-paraneoplastic autoimmune optic neuropathy with anti-recoverin antibodies.

Results:: A 44 year old woman had in 2017 an acute episode of painful rapidly progressive visual loss in her left eye. Funduscopic examination showed mild alterations of the retinal pigment epithelium and optical coherence tomography showed papilledema. She received treatment with oral corticosteroids and the visual impairment resolved completely. She consulted one year later. Visual - Evoked Potentials (VEP) revealed a demyelinating left optic neuropathy. Brain and spinal cord magnetic resonance (MRI) were normal. NMO and MOG antibodies were negative. A lumbar puncture detected oligoclonal IgG bands in CSF. In 2019 the patient reported visual loss through her right eye and was treated with corticosteroids. New VEP showed axonal right optic neuropathy. A full autoantibody panel was performed, testing positive for anti-recoverin antibodies. Malignancy screening was negative. Although the patient reports nyctalopia and occasional blurred vision, her visual acuity returned to normal.

Conclusions:: The case illustrates how heterogeneous non-paraneoplastic AIR can be. We report an atypical clinical course, presenting as a recurrent optic neuropathy responsive to corticosteroid treatment associated with mild retinal alterations. In this case, the early corticosteroid treatment could have prevented further visual loss.
HORNER'S SYNDROME DUE TO HASHIMOTO'S THYROIDITIS

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Background and Aims:: Horner’s syndrome is characterized by ptosis, ipsilateral miosis, anhidrosis and occasionally apparent enophthalmos. Amongst the diverse neoplastic and non-neoplastic causes of acquired Horner’s in children, thyroid disease is rare. We present a case in which Horner’s syndrome was a consequence of the mass effect from a substantially sized goiter due to Hashimoto’s thyroiditis.

Methods:: A 13-year-old male presented with anisocoria and partial right eye ptosis. Following ophthalmic assessment and with the aid of pharmacological tests the diagnosis of acquired Horner’s syndrome was made. The patient was otherwise fit and healthy with no other symptoms. In view of the young age, MRI of the brain, orbits, neck and upper mediastinum was conducted which identified the enlarged thyroid. Fine-needle aspiration was compatible with lymphocytic thyroiditis. In our case, it is probable that the oculosympathetic tract injury present occurred in the pre-ganglionic region.

Results:: The diagnosis of Hashimoto’s thyroiditis was made. The patient was referred to an endocrinology team and was started on oral carbimazole. A year later, the goitre had almost resolved and his thyroid function returned to normal. The ptosis and anisocoria showed little improvement.

Conclusions:: It is important to exclude neuroblastoma as it is amongst the most common childhood tumours causing acquired Horner’s in young children. In rare circumstances, thyroid disorders may be associated with Horner’s syndrome and benign diseases predominate. Although the thyroid disorders associated with Horner’s are mostly benign diseases, it is imperative that appropriate investigations and treatment approaches are conducted timely to exclude the potential of a malignancy.
INCIDENCE OF MITOCHONDRIAL MUTATIONS IN COHORT OF PATIENTS WITH ETHAMBUTOL-INDUCED OPTIC NEUROPATHY

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Background and Aims:: Background: Ethambutol-induced Optic Neuropathy (EtON) is a devastating complication of the Anti-tubercular therapy (ethambutol-based regime) which is a cornerstone for the treatment of Tuberculosis. Though the etiology of the disease is unknown yet it has been postulated to be mitochondrial associated for a long time. It is intriguing to understand the basis which will aid in recognizing the “at-risk” population. Aim and Objective: To assess the association of mitochondrial mutations in the cohort of patients with Ethambutol-induced Optic Neuropathy (EtON)

Methods:: Patients who are on ATT (Ethambutol-based regime) and developing Ethambutol-induced Optic Neuropathy are being recruited. From the collected blood sample, mitochondrial DNA will be amplified after the isolation of whole genomic DNA. PCR- RFLP method will be used to further detect the presence of three mitochondrial mutations i.e. G3460A, T14484C, and G11778A.

Results:: Association of the mitochondrial mutations with Ethambutol-induced Optic Neuropathy and with the visual prognosis of the patients will be assessed. Recognition of high-risk groups may help isolate individuals in whom a longer duration of ethambutol can be avoided.

Conclusions:: Conclusion: A subset of patients who have a high predisposition to develop EtON upon the long duration of the drug will be isolated. The exposure of the drug ethambutol may be shortened in these patients.
TO ASSESS THE LEVEL OF CYTOKINES AND CHEMOKINES IN PATIENTS OF IDIOPATHIC INTRACRANIAL HYPERTENSION (IIH)

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Background and Aims:: Background: Idiopathic intracranial hypertension (IIH) is a disorder characterized by elevated intracranial pressure (ICP) without an identifiable etiology. While, Headache, double vision and subsequently visual loss are the common symptoms, it is probably the commonest neurological cause of reversible blindness. The pathogenesis of idiopathic intracranial hypertension (IIH) remains unclear and as such it remains a diagnosis of exclusion. Aim: To measure the levels of pro and anti-inflammatory cytokines in serum and CSF of patients with IIH and study the association between inflammatory cytokines with neurological, ophthalmological and radiological profile of these patients.

Methods:: The diagnosis of IIH is being made after detailed neurologic, ophthalmic and radiological examination. 35 IIH patients and 10 controls were screened for the levels of cytokines and chemokines in the cerebrospinal fluid and serum using BD™ Cytometric Bead Array (CBA).

Results:: Result: Cytometric Bead Array showed elevated levels of IL-6, TNF α, IL-2, IL-17A, IL-10 in serum and IL-6, IL-2, IL-17 A in CSF in IIH patients compared with the controls.

Conclusions:: Conclusion: This study demonstrates differences in cytokine expression in the serum and CSF in IIH patients compared with controls. Since, the pathogenesis of IIH is unclear, the heterogeneity of the cytokine expression reported here may help understand the pathogenesis of this condition and further help in diagnosis of the disease.
CASE REPORT: A SURPRISING CAUSE OF ACUTE VISION LOSS

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Background and Aims:: Methanol poisoning is a common problem because of accidental ingestion of methanol or drinking adulterated liquor containing methanol. Exposure apart from ingestion is rare. Here we present a case in which acute vision loss occurred after inhalation.

Methods:: A 32y/o gentleman, worker in a chemical factory, presented to medical emergency with acute onset painless bilateral vision loss progressing to complete loss of light perception in 4 hours. He had inhaled fumes while working which made him feel dizzy. On presentation, he had fixed and dilated pupils and visual acuity was reported as no perception of light. Fundus examination showed bilateral optic atrophy. MRI of the brain showed hemorrhagic necrosis in bilateral putamina. Hemoglobin 14.8gm%, TLC 7300/mm³, DLC N91L8M2, Platelet count 158000/mm³, Urea 15mg/dL, Cr 1.12mg/dL, Sodium 134meq/L, Potassium 3.88meq/L, Chloride 107meq/L, Total Bilirubin 1.26mg/dL, Conjugated Bilirubin 0.23mg/dL. CSF showed 8 cells/mm³, N25L75, glucose 73mg/dl, protein 164mg/dl. He was given I.V. Methylprednisolone 1gm dailyx3 days followed by oral prednisone 1mg/kg weekly taper, high dose vitamin b12, folic acid and thiamine. His vision status did not change after 3 months of follow up.

Results:: He did not gain any useful vision even after 3 months of treatment.

Conclusions:: Poisoning by methanol even by inhalation could cause severe neurological symptoms especially severe vision loss.
Background and Aims:: Sub-acute visual loss together with optic disc oedema and macular star is referred to as neuroretinitis. Several conditions are known to masquerade as neuroretinitis. Idiopathic intra-cranial hypertension (IIHT) is one of them.

Methods:: A 35-year-old female, with a body mass index of 30.3 kg/m² presented with gradual loss of vision on the right eye over 2 weeks. She also complained of a long standing non-specific headache. Examination showed reduced visual acuity of 6/60 on the right eye with optic disc oedema and a macular star. The left eye was normal. No other neurological deficits were noted. Her blood pressure was normal. Her MRI-brain and orbits were normal. However, the CSF opening pressure was 330 mm.H₂O with normal constituents. The blood and CSF cultures were negative. The inflammatory markers were normal. Toxoplasma and HIV serology were negative. Bartonella serology was not available. She was initially treated with a combination of high-dose steroids and IV ciprofloxacin. This did not lead to a significant improvement in her visual impairment. However, following the discovery of elevated CSF opening pressure, she was commenced on acetazolamide and topiramate. This led to an improvement in the visual acuity on the affected eye to 6/24 and the optic disc oedema and macular star had reduced in size, two weeks after discharge.

Results::
Conclusions:: IIHT can rarely present with unilateral disc oedema and a macular star, mimicking neuroretinitis and cause a reduction in visual acuity, even at CSF pressures around 300 mm.H₂O.
Background and Aims:: Background: Chronic Relapsing Inflammatory Optic Neuropathy (CRION) is a rare and still poorly defined entity. Optic Coherence Tomography may improve diagnosis.

Methods:: Case report.

Results:: A 60 year old woman presented with subacute blurred vision, dyschromatopsia and pain on the right eye. Past medical history was unremarkable. On the first neurological examination pupils were equal and reactive to light, right VA was 9/10, fundus oculi examination was normal. After one month she experienced a dramatic worsening with great impairment of VA, counting fingers at 1 meter on the right. Right RAPD was present. Retinal nerve fiber layer (RNFL) was mildly increased bilaterally, VEP showed increased latency and reduced amplitude on the right, CSF electro focusing demonstrated type IV pattern. Orbit and brain MRI were normal. Anti NMO and anti MOG antibodies were negative. Doppler ultrasound of the temporal artery was negative. The patient was treated with high dose iv steroids with dramatic clinical response and RNFL thickness reduction. During steroid tapering she experienced a relapse on the right eye. OCT scan demonstrated increased RNFL thickness and GCL atrophy. The patient required continuous immunosuppression. CRION is a form of steroid responsive inflammatory optic neuropathy, which may belong to the growing family of NMOSD. Our patient experienced a subacute visual loss which developed over 2 months, with sudden acute worsening and dramatic recovery after steroids. OCT was consistent with inflammatory optic neuritis and was supportive in diagnosis.

Conclusions:: OCT may be a useful tool in diagnosing and monitoring inflammatory optic diseases.
HOMONYMOUS HEMIANOPIA IN MULTIPLE SCLEROSIS

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Background and Aims:: Ophthalmic manifestations are a prominent feature of multiple sclerosis (MS). Compared with optic neuritis retrochiasmal visual symptoms, such as homonymous hemianopia, are rare. We present an unusual case of homonymous hemianopia secondary to demyelinating process.

Methods:: A 40-year old female presented with sudden onset painless bilateral visual loss. The patient had been diagnosed with MS thirteen years earlier and had never received treatment. She had remained asymptomatic for several years. She also suffered from discoid lupus and migraines. On examination, best-corrected visual acuity was right eye 6/18 and left eye 6/9. Extra-ocular movements were normal and there was no relative afferent pupillary defect or colour vision loss. Dilated fundoscopy was unremarkable. Visual fields to confrontation suggested right homonymous hemianopia which was confirmed on automatic perimetry.

Results:: Magnetic resonance imaging on the day of presentation revealed multiple demyelinated lesions in the supratentorial region with no obvious contrast enhancement. Within days her right visual acuity reduced to counting fingers and now had a right relative afferent pupillary defect and colour vision impairment. Repeat imaging nine days following presentation, showed a lesion of the optic chiasm to the right with high T2/FLAIR signal intensity and mild contrast enhancement which was extending to the ipsilateral proximal optic tract. The patient was immediately pulsed on intravenous methylprednisolone 1gr for five consecutive days. She demonstrated excellent response to the treatment and was subsequently commenced on an immunomodulator.

Conclusions:: Homonymous hemianopia is uncommon in multiple sclerosis (0.5%-3.5%) and usually carries a favorable prognosis unlike other etiologies.
EYE BLOOD SUPPLY STUDY USING COLORED ULTRASONIC DOPPLEROGRAPHY

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Background and Aims:: The aim of the work is to study the state of blood circulation of the vessels of the eyeball in patients with atherosclerotic lesions of the carotid arteries of a hemodynamically significant nature, using the method of color Doppler ultrasound

Methods:: We examined 24 patients with atherosclerotic lesions of the carotid arteries of a hemodynamically significant nature (more than 70%) aged 51 to 74 years (16 men and 8 women)

Results:: It should be noted that the blood flow velocity obtained by us in the orbital artery and the central retinal artery was close to their results, then the maximum systolic blood flow velocity in the posterior short ciliary arteries, according to our data, significantly differs from those found by other authors, namely: from 8, 2 to 20 cm / s according to our data and 25.22 ± 4.53 cm / s. As for the final diastolic blood flow velocity, its values were close to the values obtained by the indicated authors, while maintaining a more pronounced tendency to decrease in the orbital artery. A few words about the resistance index

Conclusions:: The method of color Doppler ultrasound allows us to determine the blood flow velocity in the vessels supplying various parts of the eyeball that are inaccessible to direct observation, as well as a significant decrease in the blood flow velocity in a particular vessel feeding the eyeball
SHORT TERM AND LONG TERM VISUAL OUTCOMES IN PATIENTS OF IIH PRESENTING WITH BLURRING OF VISION

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Background and Aims:: Idiopathic Intracranial Hypertension (IIH) is a condition leading to raised intracranial pressure in the absence of any structural cause. Progressive blurring of vision is a complication of IIH and if not addressed, may lead to permanent blindness too. This study was done to assess the outcomes in patients of IIH presenting with blurring of vision to a tertiary care hospital in India.

Methods:: This was a retrospective study. Records of IIH patients presenting in last 5 years (1st January, 2016 to 31st December, 2020) with blurring of vision were assessed. Those who were regular in follow up were included in this study. The short term as well as long term visual outcomes with medical or surgical interventions were studied.

Results:: Out of 71 patients of IIH presenting to the hospital, 24 presented with blurring of vision. 3 out of 24 were lost to follow up. The remaining 21 patients were included in study. 16 patients responded to medical management (acetazolamide) whereas 5 patients required surgical procedure in addition to acetazolamide. Short term results (after 1 month therapy) showed improvement in vision in 14/16 patients on medical management and 3/5 patients on medical plus surgical management. Long term results (after 6 months of therapy) showed improved vision in all 16 patients on medicine and in 4 out of 5 patients in surgical group. 1 patient developed blindness in 2nd group.

Conclusions:: IIH is a disease having potential for permanent visual loss. Timely initiation of treatment with proper choice of treatment is required for improvement in the symptoms.
UNILATERAL OPTIC NEURITIS CAUSED BY SOLVENT. A CASE REPORT

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Background and Aims:: Optic neuritis is one manifestation of central nervous system inflammation with resultant demyelination. Inflammatory-type optic neuritis caused by solvent is a rare clinical entity. It presents as acute loss of vision attributable to the use of neurotoxic substances such as cleaning solvents for domestic use.

Methods:: we describe a rare clinical case of unilateral optic neuritis caused by solvent.

Results:: A 41-year-old woman in January 2021 had an acute episode of painful and rapidly progressive visual loss in her left eye after the use of solvent for cleaning the bathroom a few days before. She consulted and complementary tests were performed. The rest of the neurological examination was normal. Funduscopic examination showed effacement of the left eye papilla and optical coherence tomography showed diffuse thickening of the optic nerve. In the blood analysis, an acute deficiency of folic acid was highlighted. NMO and MOG antibodies were negative. The MRI showed hypercaptation in both tear glands. The patient improved without treatment until she recovered ad integrum in five days.

Conclusions:: Inflammatory-type optic neuritis caused by solvent is an entity rarely described in the literature. We present a clinical case with acute onset of symptoms after use of solvent with spontaneous resolution after eight days. Faced with optic neuritis, we must carry out a broad differential diagnosis, insisting on the anamnesis for the use of substances, even days before. The deficit of folic acid can guide us to toxicity as a cause.
MISSING TISSUES IN EYE AND HEART WITH FACIAL PALSY - CASE REPORT OF CHARGE SYNDROME WITH LATE PRESENTATION AS HEART FAILURE

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Background and Aims:: CHARGE syndrome is a rare multisystem genetic disorder. Mutation in CHD7 gene was seen in around 58-64% of cases. It is usually diagnosed in infancy or childhood owing to the characteristic clinical features. However, there are occasionally late presentations, especially in resource limited settings where the clinical features may be ignored by the patients and there is delay in seeking medical care. We report a case of CHARGE syndrome with late diagnosis presenting with heart failure.

Methods:: CASE PRESENTATION: A 24-year-old male presented with exertional breathlessness, orthopnea and paroxysmal nocturnal dyspnea for 1-month duration. He was born out of non-consanguineous marriage and had normal antenatal and perinatal periods. He had mild developmental delay in motor milestones and difficulty in vision. However, he did not get evaluated earlier. There was no significant family history. On examination, he had short stature, microcornea, coloboma of iris and retina, external ear anomaly, prognathism, hockey-stick palmar crease and left facial palsy. Cardiac system examination suggested heart failure.

Results:: Routine blood investigations were normal. Echocardiography showed ostium secundum atrial septal defect and features of pulmonary artery hypertension. He was diagnosed as having CHARGE syndrome based on the clinical findings. Genetic studies couldn't be done due to financial constraints. He was treated with diuretics for cardiac failure and planned for atrial septal defect closure.

Conclusions:: It is a disease which needs early diagnosis as it involves multiple systems and requires early multi-modality intervention. The characteristic clinical features, which if recognized early will help in early diagnosis and management of this condition.
VISUOCOGNITIVE IMPAIRMENT IN MULTIPLE SCLEROSIS: THE RELATIONSHIP BETWEEN NEUROPSYCHOLOGICAL AND EVOKED POTENTIAL MEASURES

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Background and Aims::
Visual evoked potentials (VEPs) and event-related potentials performed with visual stimulation (VERPs) can be recorded non-invasively from different regions of the scalp. To compare simultaneously recorded VEPs and VERPs in MS patients without visual impairment.

Methods::
We performed a study of simultaneously recorded “primary” (VEPs) and “cognitive” (ERPs) visual evoked potentials in a group of MS patients who have no signs or symptoms of visual dysfunction. Two unidimensional Gabor patches of 1 cycle per degree of spatial frequency, differing in the orientation of the gratings, were presented in an “odd-ball” paradigm to 30 patients with MS and 30 age-matched control subjects. We measured latencies and amplitudes of N70, P100, and P300 components, deriving the “normalized” measures of P300-N70 latency difference (Central Processing Time - CPT70), the P300-P100 latency difference (CPT100), and the P300 amplitude responses normalized to either N70 and P100 amplitude.

Results::
We evaluated the relationship between primary and cognitive processing abnormalities. Then we investigated whether or not patients with orientation-dependent VEP changes, which are thought to be due to cortical pathology, have VERPs abnormalities. Third, we investigated if individual orientation-specific VEPs and VERPs results correlate with selective neuropsychological test scores for visuoperceptual or visuospatial skills. A wide battery of neuropsychological tests was performed. We found a significant correlation (r=066, p<0.01) only between the Stroop test and the raw and normalized (CPT) P-300 results.

Conclusions::
Simultaneously recorded VEPs and VERPs in MS patients are a promising tool for the study of cognitive function in MS.
ATYPICAL VISUAL IMPAIRMENT ASSOCIATED TO CEREBRAL SINUS STENOSIS RELATED TO COVID 19 THROMBOSIS

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Background and Aims:: Cerebralvenoussinus stenosis (CVSS) may further complicate cerebral venous thrombosis(CVT) which is a rare thromboembolic complications in COVID-19 patients. We report a case of post COVID 19 CVT-related CVSS associated to intracranial hypertension (ICH). We discuss the possible mechanisms of highly asymmetric visual repercussions of ICH.

Methods:: A 45-year-old woman presented with complains of isolated visual loss in the right eye (RE). Her medical history included COVID-19 CVT for the past month. Visual acuity was 2/10 in the RE and 10/10 in the left eye. Fundus examination revealed bilateral papilledema, more important in the RE. The ultrasound examination showed right ON calcifications. Brain MRI showed features of raised intracranial pressure and revealed incidentally an extra axial meningioma surrounding the left ON in its retrobulbar portion. Brain MRA showed right lateral sinus stenosis. Lumbar puncture revealed significantly elevated intracranial pressure. Endovascular stenting was proposed.

Results:: CVSS can cause chronically-ICH. Patients may have no neurological symptoms other than visual impairment, secondary to bilateral papilledema. In this case, the visual repercussions of ICH were highly asymmetric. Compartmentalized cerebrospinal fluid would be a possible mechanism for asymmetric papilledema. The meningioma of the left ON could protect optic fibers from increased intracranial pressure. The ON head drusens of the RE would be an aggravating factor.

Conclusions:: Clinicians should consider the risk of CVT in the COVID-19 pandemic. Ocular symptoms could be the initial signs of CVSS. Correctly recognizing this condition is very important to avoid delayed treatment and complications.
**Background and Aims:** Mycoplasma pneumoniae (MP) is an atypical bacterium that can cause a variety of respiratory infections as well as neurological and ocular involvement such as conjunctivitis, third or sixth nerve palsies, uveitis and rarely optic neuropathy (ON).

**Methods:** A 38-year-old woman had a typical retrobulbar ON of the right eye, treated with corticosteroid therapy at high doses. Visual acuity improved to 16/20 after 5 days. One week later, she consulted for visual loss of the same eye at 6/20 associated with conjunctivitis. Neurological examination and brain MRI showed no abnormalities. A history of neglected respiratory infection was found with no evidence of other infection or auto-immune disease. The diagnosis of MP infection was established due to the presence of MP specific IgM antibodies. The patient was treated with corticosteroids and fluorquinolones. Outcome was favorable with complete regression of symptoms, and no recurrence after a follow-up of 4 years.

**Results:** The pathologic mechanism of extra-pulmonary involvement of MP remains unclear but is thought to be the result of direct invasion of the central nervous system, or a post infectious immune response. The coexistence of respiratory and visual symptoms with high levels of MP specific IgM antibodies underlines the possibility that the two infectious and auto-immune mechanisms are concomitant. This suggestion could justify antibiotic and steroid combination therapy and may explain initial improvement with corticosteroids in our case.

**Conclusions:** Atypical optic neuritis in a young adult should prompt consideration of a serologic testing for MP infection especially in endemic regions.
TOLOSA-HUNT SYNDROME: A RARE ENTITY

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Background and Aims:: Tolosa Hunt syndrome (THS) is an inflammatory process adjacent to the cavernous sinus or within the superior orbital fissure and/or orbital apex. It is a rare entity well-defined clinically but of unknown etiopathogenesis.

Methods:: A 26-year-old woman presented with painful eye movements and diplopia. Examination revealed left ophthalmoplegia, ptosis with exophthalmos. Visual acuity was 7/10 in the left eye, 10/10 in the right eye. Fundoscopic examination was normal in both eyes. The remainder of the neurologic examination was unremarkable. Brain MRI revealed left orbital apexitis with diffusely enhancing left orbital apex extending to the anterior cavernous sinus and oculomotor muscles. The immunological and infectious assessments were negative. The diagnosis of THS was made, and the patient received corticosteroids. Outcome was favorable with complete regression of oculomotor symptoms after few days of treatment.

Results:: The clinical diagnostic criteria of THS include an episode or episodes of unilateral orbital pain; paralysis of one or more of the third, fourth, and sixth cranial nerves; and resolution of symptoms within 72 hours after corticosteroid therapy, with exclusion of other causes. MRI findings show inflammatory changes within anterior cavernous sinus, with or without involvement of the internal carotid artery, superior orbital fissure, orbital apex and optic nerve.

Conclusions:: Although THS is often a benign condition, it may lead to optic nerve involvement and blindness. Therefore, it is important to recognize the clinical features of this disease and provide immediate treatment to preserve visual function.
DRAMATIC TRAUMATIC OPTIC NEUROPATHY: A RARE ENTITY

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Background and Aims:: Traumatic optic nerve (ON) avulsion corresponds to the disinsertion of the ON from the eyeball at the level of the lamina cribrosa. We report clinical and multimodal imaging findings in partial (ON) avulsion following head trauma.

Methods:: An 11-year-old boy presented with complains of sudden vision loss of the left eye (LE) following blunt trauma with a wooden stick.

Results:: Examination of the LE found visual acuity limited to counting fingers and an afferent pupillary defect. Fundus examination showed superficial and deep peripapillary hemorrhages as well as retrohyaloid hemorrhages. A deep depression with empty space at the inferior pole of the ON head was noted. Brain MRI was without abnormalities. Kinetic perimetry found a superior altitudinal deficit in the LE. Optical coherence tomography (OCT) showed an interruption of axons at the inferior-temporal edge of the ON head with thinning of retinal nerve fiber and ganglion cell layers.

Conclusions:: In ON avulsion, the ON is disinserted from the retina, and the lamina cribrosa is retracted from the scleral rim. This is a rare and dramatic form of direct traumatic optic neuropathy. ON avulsion usually results from sudden extreme rotation or anterior displacement of the globe following head trauma. The diagnosis is evident in fundoscopy. OCT could reveal the disruption of ON axons at the scleral rim. The prognosis for this disease remains very poor. Its therapeutic management remains to date non-consensual.
**A RARE PRESENTATION OF MYASTHENIA GRAVIS FOLLOWING BOTULINUM TOXIN INJECTION**

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**Background and Aims::** Botulinum toxin drugs have an excellent safety profile. Adverse events are most often related to the local diffusion of the toxin and are usually mild and transient. However, there are cases where the clinical manifestations following the injection cannot so easily be explained. We describe a case of myasthenia gravis following periocular botulinum injection.

**Methods::** The patient presented with sudden onset diplopia ten days after botulinum toxin injection. There was also mild right sided ptosis which the patient first noticed five years earlier. The symptoms were initially attributed to the local diffusion of the drug, but her diplopia persisted beyond three months. Further, the diplopia constantly fluctuated requiring frequent revision of her Fresnel prisms.

**Results::** MRI orbits and brain and routine blood investigations were all normal. The blood test for antibodies (Ab) against acetylcholine receptor (AChR) and muscle-specific kinase (MUSK) were done: AChR Ab was negative and MUSK Ab was positive. Computer tomography showed no thymoma and spirometry was normal. In view of the emerging clinical picture and blood results, a diagnosis of myasthenia gravis with MUSK Ab was made. A year later, she remains well controlled on treatment, and even her ptosis has improved, but her symptoms occasionally relapse during her menstrual cycles.

**Conclusions::** Botulinum toxin injection may unmask subclinical generalized myasthenia gravis, therefore clinicians should be vigilant of this possibility. In patients with pre-existing neuromuscular pathology or signs of muscle weakness such as the ptosis in our patient, botulinum toxin should be used with caution.
OCULAR ISCHEMIC COMPLICATIONS FROM RETINAL MIGRAINE

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¹Mayo Clinic, Neurology, Scottsdale, United States of America, ²Mayo Clinic, Ophthalmology, Scottsdale, United States of America, ³Mayo Clinic, Neurology, Rochester, United States of America

Background and Aims:: Retinal migraine is defined by ICHD 3rd edition as fully reversible monocular visual phenomena, accompanied, or followed within 60 minutes by headache. We report two patients with persistent visual phenomena that complicated with either severe disabling visual loss or permanent visual field defect. We emphasize the importance of retinal migraine acute and preventive management.

Methods:: Case-series

Results:: Case 1. 57-year-old man with longstanding history of bi-annual retinal migraines and hypertension controlled on a calcium-channel blocker, presented with painless monocular visual loss. Initial symptoms were reminiscent of his typical retinal migraines, however progressed over 4 days to right eye finger-count vision. Intravenous fluorescein angiography (IVFA) showed paracentral acute middle maculopathy at 48-hours, and combined central retinal vein and central retinal arterial occlusion at 96-hours after onset. He was prescribed preventative daily nortriptyline and magnesium, and acute sublingual nitroglycerin should he experience contralateral visual auras. Case 2: 21-year-old man with history of one retinal migraine and family history of migraines, presented with a 24-hour persistent right eye supero-temporal scotoma after a retinal migraine. Visual acuity was normal; a right relative afferent pupillary defect and right supero-temporal visual field defect were noted, consistent with ischemic optic neuropathy. Daily migraine preventive therapy was recommended.

Conclusions:: Retinal migraines are not benign conditions, as they can complicate with retinal or optic nerve infarction. Migraine prophylactic therapy should be recommended to prevent disabling visual loss even in subjects with infrequent retinal migraines, especially with monocular vision. Patients should have a low threshold to self-administer early acute migraine therapy.
PROFILE OF DISC ATROPHY IN CIPTO MANGUNKUSUMO NATIONAL HOSPITAL

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Faculty Faculty of Medicine University Indonesia- Cipto Mangunkusumo hospital, Departement Of Neurology, Jakarta, Indonesia

Background and Aims:: Disc atrophy is the end stage of the degeneration of the optic nerve. It is divided into primary and secondary disc atrophy. This study aimed to describe the etiologies and the characteristics of disc atrophy in Neurology Outpatient Clinic, Cipto Mangunkusumo Hospital, Jakarta.

Methods:: This retrospective cross-sectional study performed in Neuroophthalmology-Neurootology Diagnostic Clinic of Cipto Mangunkusumo Hospital, Jakarta, 2014-2019. Statistical analysis of Chi-square/Fisher exact test and Mann-Whitney test

Results:: Of 1,821 patients included in this study, 278 patients (6.5%) presented with disc atrophy. Primary disc atrophy proportion was 81.7% and usually unilateral whereas secondary disc atrophy was 20.8% and bilateral. Both primary and secondary disc atrophy showed a pupillary abnormality, a severe degree of visual acuity impairment, and visual field defect. The visual acuity tends to be a blindness in primary optic atrophy (72.6%) and secondary optic atrophy (80.7%). The severity of visual acuity was significantly more severe in secondary optic atrophy (Logmar 2.24±0.95 vs 1.94±0.99, p 0.005). Moreover, the proportion of complete visual field defects was significantly higher in secondary disc atrophy (90.5% vs 52.3%, p 0.00). CNS tumor commonly found as an etiology in secondary disc atrophy than primary (54.9% vs 28.2%, p 0.001). Ischemic optic neuropathy (13.7%, p 0.002) and multiple sclerosis/NMO (8.4%, p 0.03) were found only in primary disc atrophy.

Conclusions:: Different characteristics and etiologies occurred in primary and secondary disc atrophy. The visual acuity impairment and visual field defect were more severe in secondary disc atrophy. In regard to the etiology, CNS tumor found commonly in secondary disc atrophy, whereas ischemic optic neuropathy and multiple sclerosis/NMO found commonly in primary disc atrophy.
Background and Aims:: Fundoscopy is a useful tool in diagnosing neuro-ophtalmology disorders, especially for detecting papilledema and optic disc edema. However, there is a risk of airborne transmission that should be considered before doing the examination. Some clinical characteristics may help in deciding to do a fundoscopy examination.

Methods:: We analyzed a retrospective database consisting of 973 patients that were examined in a neuro-ophtalmology clinic at dr. Cipto Mangunkusumo Hospital, the national referral hospital of Indonesia, during the period of 2016-2019. Statistical analysis was done using SPSS.

Results:: Optic disc edema was found in 1.3% of patients. The visual complaint was more likely to be impaired visual acuity (p=0.005) and often accompanied by orbital pain (p=0.012). The most likely etiology was ischemic optic neuropathy (38%, p<0.001). Papilledema was found in 10.3% of patients. Visual complaints in patients with papilledema were more likely to be diplopia (p=0.031), persistent (p=0.004), and accompanied by a focal neurological deficit (p=0.008). The most frequent etiologies causing papilledema were brain tumor (51%, p<0.001) and CNS infection (7%, p=0.019). There was no significant difference of visual loss distribution (unilateral or bilateral) and onset, both in disc edema and papilledema.

Conclusions:: Some clinical characteristics and known etiologies can help neuro-ophtalmologists to prioritize patients for fundoscopy examination, particularly in office settings amid the COVID-19 pandemic.
POST COVID-19 OPTIC NEURITIS: TWO EGYPTIAN CASE REPORTS

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¹kasralainy cairo university, Clinical Neurophysiology, cairo, Egypt, ²Cairo University, Clinical Neurophysiology, cairo, Egypt

Background and Aims:: The exact incidence of neurological complications from coronavirus disease 2019 (COVID-19) infection is still unknown. Neurological symptoms are more common with severe form of the disease. Through neuro-invasion, the virus can affect both neurons and glial cells and induce wide range of neurological pathologies. CNS symptoms are more common representing 91% of all neurological patients with 9% only with PNS. PNS manifestations showed variable results, where visual impairment and nerve pains were more frequent in the severe COVID-19 category of patients.

Methods:: This is a two-case report of post COVID optic neuritis, both after severe COVID infection and hospitalization, they developed acute onset visual affection mostly one and a half month in the first case and two months in the second one after almost complete cure. The first case had delayed perception of vision, the second one had complete visual loss of one eye of unexplained causes.

Results:: All neurological and ophthalmological investigations were normal apart from pattern visual evoked potentials that showed small amplitude P100 response bilaterally in the first case and absent pattern and flash VEP responses on the clinically affected side in the second case.

Conclusions:: This supports what was stated in a study based on murine models of other CoVs, which stated that viral-induced optic neuritis secondary to autoantibody production against neuroretina should also be considered and suggested that infected patients should be monitored for signs of neuroretinal degeneration on the long term.
PHARMACOACUPUNCTURE THERAPY FOR DIZZINESS IN TRADITIONAL KOREAN MEDICINE: A SYSTEMATIC REVIEW

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Kyung Hee University Korean Medicine Hospital, Stroke Center, Seoul, Korea, Republic of

Background and Aims: This systematic review aimed at briefly exploring how effective pharmacoacupuncture therapy for dizziness is.

Methods: We searched publications in Medline, EMBASE, Cochrane Library, KoreaMed, China National Knowledge Infrastructure (CNKI), Cinii, DBpia, KSI, Kiss, KMBase, NDSL and RISS. We included randomized controlled trials and well-designed non-randomized controlled trials that compared the effects of only pharmacoacupuncture or pharmacoacupuncture and usual therapies with any controls for dizziness.

Results: The risk of bias was assessed using the Cochrane tool. Three studies have been included with eligibility criteria (Fig 1). Risk of bias assessments showed mostly “unclear” because the included study reported the results poorly (Fig 2). This review found the evidence that pharmacoacupuncture therapy was effective as add-on therapy to acupoint therapy, physiotherapy and had additional benefits in increasing of CER for cervical vertigo. Also, it was recommended that pharmacoacupuncture therapy was effective as add-on therapy to western medicine and had additional benefits in increasing of CER for vasovagal syncope (Table 1).
Fig 1 PRISMA diagram for the included
### Fig 2 Risk of bias assessment. Table 1 Key Data for included Trials on Pharmacoacupuncture for treating Dizziness

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<tr>
<td>Random sequence generation (selection bias)</td>
<td>?</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>?</td>
<td>+</td>
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<tr>
<td>Blinding of participants and personnel (performance bias)</td>
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<td>Blinding of outcome assessment (detection bias)</td>
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<td>Incomplete outcome data (attrition bias)</td>
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<td>Other bias</td>
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**Conclusions:** Pharmacoacupuncture therapy had additional benefits as add-on therapy for cervical vertigo and vasovagal syncope. However, further studies are required to overcome the limitations of lack of study qualities.

<table>
<thead>
<tr>
<th>Study ID</th>
<th>P</th>
<th>Study design</th>
<th>Intervention (I)</th>
<th>Comparison (C)</th>
<th>Duration</th>
<th>F/U</th>
<th>Outcome measurements</th>
<th>Results</th>
<th>Adverse events</th>
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<tr>
<td>Gao 2000</td>
<td>Cervical vertigo</td>
<td>RCT</td>
<td>PA(Danshen zhusheye 4ml) plus MX GB20 and GV 14 (n=42)</td>
<td>AT, GB20 and Cervical Hyeopcheck point (n=42)</td>
<td>30days</td>
<td>X</td>
<td>CER</td>
<td>40/42 vs 35/42 (95.24% vs 83.33%)</td>
<td>No report</td>
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<tr>
<td>Wang 2008</td>
<td>Cervical vertigo</td>
<td>RCT</td>
<td>PA(Xiangdan zhusheye) plus physiotherapy GB20 and Cervical Hyeopcheck point (n=34)</td>
<td>physiotherapy (n=34)</td>
<td>20days</td>
<td>X</td>
<td>CER</td>
<td>24/34 vs 15/34 (94.1% vs 76.4%)</td>
<td>No report</td>
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<tr>
<td>Liu 2012</td>
<td>Vasovagal syncope</td>
<td>non-RCT</td>
<td>PA(Huangqi zhusheye) plus WM(Metoprolol) ST36 (n=20)</td>
<td>WM/Metoprolol (n=20)</td>
<td>3months</td>
<td>after 6months</td>
<td>CER</td>
<td>18/20 vs 14/20 (90% vs 70%)</td>
<td>No report</td>
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QUALITATIVE STUDY EXPLORING CLINICIANS’ EXPERIENCE OF PARTICIPATING IN A FEASIBILITY TRIAL INVESTIGATING BENIGN PAROXYSMAL POSITIONAL VERTIGO IN TRAUMATIC BRAIN INJURY

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Background and Aims:: This is a multi-centre qualitative study embedded within a larger multiphase feasibility study investigating the management benign paroxysmal positional vertigo (BPPV) in acute traumatic brain injury (TBI). Evidence has shown qualitative methods have a place in feasibility studies as they can improve validity of a future trial. Our primary objective was to explore the acceptability of trial processes such as recruitment, randomisation and interventions. A secondary objective was to identify any facilitators or barriers to implementing a more definitive randomised controlled trial (RCT).

Methods:: A qualitative approach was utilised as it provides an interpretive view of context-related phenomena. We used the theoretical domains framework to inform our topic guide and provide a theoretical lens into factors affecting behaviour. Participants from the research team across two major trauma hospitals in London, UK were recruited using purposive sampling. Semi-structured, individual interviews were used as the data collection method. Data was transcribed verbatim and analysed using Framework analysis.

Results:: Eight clinicians participated: four research nurses, three physiotherapists and one occupational therapist. Concerns were raised surrounding the randomisation of BPPV patients to the usual care treatment arm. Reported facilitators included a split clinical-research post, which enabled therapists to complete study specific research activities without significant impact on their clinical workload.

Conclusions:: This work provides insight into clinicians’ perspectives of trial processes and demonstrates the importance of gaining such views. These data will inform the design of a future RCT and will help shape targeted theory-based implementation strategies for clinical behaviour change, with potential to translate into improved patient outcomes.
Galvanic Vestibular Stimulation Improves Spatial Cognition After Unilateral Labyrinthectomy in Mice

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Background and Aims:: The present study was aimed to investigate the contributions of unilateral vestibular deafferentation to spatial cognition and the efficacy of galvanic vestibular stimulation (GVS) for recovery of these deficits using a unilateral labyrinthectomized (UL) mouse model.

Methods:: Thirty-six male mice were divided into 3 groups comprising a control group and two UL groups with (GVS group) and without GVS intervention (non-GVS group). After surgical UL, locomotor and cognitive behavioral recoveries on postoperative days (PODs) 3, 7 and 14 were assessed by open field (OF), Y maze, and Morris water maze (MWM) tests.

Results:: Locomotion and spatial cognition were significantly impaired after UL (non-GVS group) compared to the control group. GVS intervention after UL significantly improved locomotion compared to control and non-GVS groups at PODs 3 and 7 in the OF and Y maze tests. Spatial working memory assessed by the Y maze were also significantly improved in the GVS group compared to the non-GVS group at POD 3. In addition, the recovery of long-term spatial navigation deficits during the MWM, as indicated by the escape latency and the probe trial, was significantly better in the GVS group compared to the non-GVS group 2 weeks after UL. (Please see the attached file)

Conclusions:: Acute unilateral peripheral vestibular lesions cause deficits in spatial cognition and motor coordination. Our study provides evidence that an early intervention with GVS was effective in improving spatial memory and navigation as well as locomotor function, implying a promising potential to rehabilitate these impairments in patients with acute unilateral vestibular failure.
SUDDEN UNILATERAL HEARING LOSS AND VERTIGO DUE TO POSTERIOR INFERIOR CEREBellar ARtery TERRITORY hypoperfUSION BY VERTEbral ARtery DISsection

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Background and Aims:: Sudden hearing loss and vertigo are the typical presentation of anterior inferior cerebellar artery infarction, but may occur in posterior inferior cerebellar artery (PICA) infarction. However, it is known that it is very rare that hearing loss and vertigo occur due to perfusion deficits without the occurrence of infarction. Here I describe a patient who presented with sudden hearing loss in left ear and vertigo due to PICA territorial hypoperfusion without infarction by vertebral artery (VA) dissection.

Methods:: case report

Results:: A 51-year-old man presented to emergency room complaining that he had suddenly lost hearing in his left ear. He had also noted vertigo and imbalance. On examination he had vibration induced right-beating nystagmus and left-beating nystagmus after head shaking test. Also he had left-beating nystagmus in right roll test and right-beating nystagmus in left roll test. The head impulse test was normal. Brain MRI showed left PICA territorial perfusion deficits without infarction. Brain MRA and conventional angiography revealed occlusion of left post-PICA intracranial VA with flow arrest and multifocal stenosis of right intracranial VA suggesting both VAs dissection.

Conclusions:: In this case, there was sudden hearing loss and severe vertigo in the early stages. If MRI/A including perfusion image was not performed, the diagnosis and treatment of cerebellar ischemia may have been delayed. Therefore, it is necessary to consider the possibility of a central cause in patients with sudden hearing loss and vertigo, and it is important to confirm through brain MRI/A including perfusion weighted image.
MENIERE’S DISEASE-LIKE SYMPTOMS IN 22Q11.2 DELETION SYNDROME

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Background and Aims:: 22q11.2 deletion syndrome (22q11.2DS) caused by a microdeletion on the long arm of chromosome 22, is characterized by congenital heart disease, hypoparathyroidism, immunodeficiency, developmental delay, and velopharyngeal insufficiency. Anatomic malformations of the middle and inner ears are frequently present, leading to high prevalence of hearing impairment. We present a first case of 22q11.2DS showing fluctuating hearing loss with recurrent vertigo attacks, resembling Ménière’s disease.

Methods:: We described clinical features and neuro-otological findings of a 38-year-old male known to have 22q11.2DS who presented recurrent vertigo, tinnitus, and fluctuating hearing loss. We also performed delayed 3D-FLAIR MRI sequences to evaluate endolymphatic hydrops of inner ears.

Results:: The patient developed recurrent vertigo, tinnitus, and fluctuating hearing loss in the left ear during a 10-year follow up period. During vertigo attack, he had spontaneous left-beating nystagmus with downbeat components, but bithermal caloric and video head impulse tests showed normal vestibulo-ocular reflex functions. Sequential pure tone audiograms demonstrated fluctuating sensorineural hearing loss (SNHL) in both ears, which finally progressed to permanent hearing loss in the left ear. Computed tomography imaging of the temporal bone exhibited bilaterally malformed lateral semicircular canals, and delayed 3D-FLAIR sequences revealed cochlear endolymphatic hydrops with dilation of the scala media in the left ear.

Conclusions:: This case shows that acute vertigo with SNHL can be one of the audiovestibular presentations in 22q11.2DS caused by disturbance of endolymphatic flow.
ISOLATED VESTIBULAR SYNDROME WITH “DOUBLE-PANDA” SIGN IN CNS LYMPHOMA

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Background and Aims:: Here we report two patients with CNS lymphoma of whom showed “double-panda” sign on MRI and developed isolated vestibular syndrome.

Methods:: Case 1: A 65-year-old male presented with acute dizziness for 3 days. He revealed bilateral horizontal GEN and catch-up saccades during bedside HITs. Brain MRI showed “double-panda” sign. Whole-body F-18 FDG PET was normal. CSF analysis exhibited mild lympho-dominant pleocytosis with elevated protein level and normal glucose ratio. One month later, he readmitted with sudden decreased mentality and received external ventricular drain due to obstructive hydrocephalus. Case 2: 77-year-old male with known DLBCL developed progressive diplopia and gait disturbance for 1 month. He showed horizontal GEN during rightward gaze and catch-up saccades during bedside HITs. Brain MRI showed “double-panda” sign. Cerebrospinal fluid analysis revealed lympho-dominant pleocytosis with markedly elevated protein level.

Results:: Both patients had horizontal GEN during bilateral (patient 1) or rightward (patient 2) gaze, and impaired horizontal smooth pursuit bilaterally. Video HITs revealed decreased VOR gains of both horizontal and posterior (patient 1) or all (patient 2) SCCs with corrective catch-up saccades. Ocular VEMPs were decreased during right ear stimulation, while cVEMPs were symmetric. Patient 2 had a canal paresis of 44.1% in the right ear on bithermal caloric tests and diagnosed with diffuse large B-cell lymphoma, histopathologically.

Conclusions:: Our cases are unique since they showed “double-panda” sign and presented isolated vestibular syndrome with characteristic findings involving the vestibular nucleus, which has been rarely described in CNS lymphoma.
ETIOLOGIC DISTRIBUTION OF DIZZINESS AND VERTIGO IN A REFERRAL-BASED DIZZINESS CLINIC IN SOUTH KOREA

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Background and Aims:: This study aimed to determine the etiologic distribution of dizziness/vertigo according to age and sex in Koreans by analyzing the diagnoses with dizziness/vertigo in a referral-based dizziness clinic run by neurologists in South Korea.

Methods:: We analyzed the diagnoses of 21,166 consecutive dizzy patients (12,691 women, mean age = 57.9±15.7, age range = 3-97) seen from 2003 to 2019 using a registry and medical records.

Results:: Overall, dizziness and vertigo were more common in women (60.0%) than in men without a difference in age (57.7±15.5 vs. 58.1±16.1, p=0.094). Benign paroxysomal vertigo (BPPV, 24.1%) was the most common cause of dizziness/vertigo, followed by psychiatric or persistent postural perceptual dizziness (20.8%), vascular disorders (12.9%), vestibular migraine (10.2%), Meniere’s disease (7.2%), vestibular neuritis (5.4%). These six disorders comprised more than 80% of all disorders. The etiology could not be determined in 5.0%, and more than one etiology were found in 14.1%. Vestibular migraine was the most common disorder in children and adolescents (<19 years), psychiatric or persistent postural perceptual dizziness (26.3%) in the adults (19-64 years), and BPPV (28.2%) in the elderly (≥ 65 years).

Conclusions:: Our study showed various causes of dizziness/vertigo in a referral-based dizziness clinic in South Korea, but only six disorders accounted for more than 80% of all diseases. This etiologic distribution is similar to that reported in another country, and indicates no significant differences in the proportion of diseases causing dizziness and vertigo across different ethnic groups. This study provides valuable information to establish healthcare policy for dizziness and vertigo.
MOTION SICKNESS SUSCEPTIBILITY AND ANXIETY/DEPRESSION MAY INFLUENCE THE ABILITY TO UPDATE ORIENTATION IN THE HORIZONTAL PLANE IN HEALTHY SUBJECTS

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Background and Aims:: To assess the ability to update orientation after passive rotations in the horizontal plane of young and middle-aged adults, considering individual factors.

Methods:: After ethical approval, 81 subjects (mean age 40.0± standard deviation 11.0 years), with no history or evidence of otology/neuro-otology/neurology disease, participated in the study. They completed an in-house general health/habits questionnaire, the motion sickness questionnaire by Golding and the Hospital Anxiety and Depression Scale (HADS). Blindfolded and wearing headphones, they were exposed to 10 manually driven whole-body rotations (45°, 90° & 135°) in a small square room with distinctive features on the walls, in such a way that the features and corners subtended 45° with respect to the subject. After each rotation, subjects reported which wall or corner they were facing. To calculate the error of estimation, the perceived rotation was subtracted from the actual rotation.

Results:: The motion sickness total score was from 0 to 27 (4.8±5.2) and the HADS score was from 0 to 30 (6.4 ±6.7). The mean estimation error was 16.6°±9.4° and the mean of correct estimations was 6.5±1.8. The performance was unrelated to age, gender, occupation, education, tobacco/alcohol consumption or sleep hours. However, factorial regression showed independent correlation of the motion sickness and HADS scores with both the mean estimation error and the total correct estimations (R= 0.37 & 0.39 respectively, p<0.01).

Conclusions:: In young and middle-aged healthy adults, motion susceptibility and anxiety/depression symptoms may influence the ability to update orientation after passive rotations in the horizontal plane.
ATTENTIONAL NETWORK DYSFUNCTION IN VESTIBULAR MIGRAINE

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Background and Aims:: Despite vestibular migraine being amongst the commonest causes of episodic vertigo, the pathophysiology remains largely unknown. Given the common complaint of spatial disorientation in vestibular migraine patients, we postulated that this may be mediated by a dysfunctional attentional network.

Methods:: We used the Attentional Network task, where participants were instructed to indicate the direction (right/left) of a target arrow in the upper or lower visual hemifield presented on a laptop screen placed 25cm away. Targets were preceded by 1 of 4 possible cue types: none, double, central, or spatial and participants were required to detect the direction of a “target arrow” that allows interrogation of three attentional networks, alerting, orienting and executive control.

Results:: Vestibular dysfunction induces a global deficit in attentional processing as reflected by significantly increased reaction time, irrespective of stimulus condition, when compared to controls. Furthermore, a clinically relevant and domain specific deficit is observed within the executive control network of VM patients.

Conclusions:: Our findings revealed a specific and clinically relevant deficit in the executive control network of vestibular migraine patients.
VIDEO HEAD IMPULSE TEST FINDINGS IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

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Background and Aims:: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder affecting upper and lower motor neurons. We examined vestibulo-ocular reflex (VOR) characteristics in ALS as examined by the video-head impulse test (v-HIT).

Methods:: We performed three dimensional vHIT in 16 patients with definite ALS (mean age 62.0±7.3 years) and 16 age-matched healthy controls. VOR gain, refixation saccade prevalence and the first-saccade amplitude, onset-latency, peak velocity and duration were examined and compared against controls.

Results:: The mean disease duration was 1.6±2.0 years and 56.2% of patients had bulbar onset. 6/16 (37.5%) patients reported history of gait imbalance resulting in recurrent falls in 3/16 (18.7%). Mean ALS-functional rating scale (ALS-FRS) score was 37.1±7. Horizontal, anterior and posterior canal (HC, AC, PC) v-HIT gains for ALS were 1.07±0.1, 0.90±0.2, 0.80±0.1 and for controls were 0.98±0.1, 0.87±0.1, and 0.85±0.1. Refixation saccade prevalence for HC, AC, PC were 67%, 20%, 70% in ALS, and 65%, 18% and 25% in controls. PC VOR gain was reduced (mean-2SD) in 6/16 (37.5%) of patients. The first-saccade amplitude and peak velocity were higher in HC and PC plane in patients with ALS compared to controls (p<0.05). There was no significant association between reduced VOR gain and ALS-FRS score.

Conclusions:: Reduction in the Posterior-Canal VOR gain with a higher than normal prevalence of refixation saccade observed in patients in ALS may represent brainstem involvement. Larger studies in patients with predominantly bulbar presentations will clarify the utility of VOR testing in ALS.
FRONTAL WHITE MATTER INTEGRITY AND IDIOPATHIC DIZZINESS IN CEREBRAL SMALL VESSEL DISEASE

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Background and Aims:: Three in ten older people (>60 years) complain of persistent dizziness which often remains unexplained despite specialist assessment and vestibular tests. The pathophysiology of such idiopathic dizziness in older people has remained unclear. We investigated if idiopathic dizziness was associated with vascular injury to white matter tracts relevant to balance or vestibular self-motion perception in sporadic small vessel disease.

Methods:: We prospectively recruited 38 vestibular clinic patients with idiopathic dizziness (median 77 years) and 36 asymptomatic controls (median 76 years) who underwent clinical, cognitive, balance, gait and vestibular assessments, and structural and diffusion brain MRI.

Results:: Patients had more vascular risk factors, poorer balance and worse executive cognitive function in association with greater white matter hyperintensity in frontal deep white matter, and lower fractional anisotropy in the genu of the corpus callosum and the right inferior longitudinal fasciculus. Tracts with lower fractional anisotropy in idiopathic dizziness overlapped with those in which lower fractional anisotropy correlated with worse balance across participants. More vestibular symptoms correlated with worse balance in patients. Vestibulo-ocular reflex and perceptual vestibular function was similar in patients and controls, though a white matter network involved in vestibular perception had lower connectivity in patients.

Conclusions:: Our results show a relationship between lower microstructural integrity in frontal balance-relevant white matter tracts in cerebral small vessel disease, poorer balance and idiopathic dizziness. This suggests cerebral small vessel disease may be involved in the pathogenesis of dizziness in some older people.
Background and Aims:: To examine the hypothesis that small vessel disease disrupts postural neural networks in older adults with unexplained dizziness in the elderly (UDE).

Methods:: Simultaneous electroencephalography and postural sway measurements were undertaken in upright, eyes closed standing, and sitting postures (as baseline) in 33 older controls and 36 older patients with UDE. Older adults underwent magnetic resonance imaging to determine whole brain white matter hyperintensity volumes, a measure of small vessel disease. Linear regression was used to estimate the effect of instability on electroencephalographic power and connectivity.

Results:: Ageing increased theta and alpha desynchronisation on standing. In older controls, delta and gamma power increased, and theta and alpha power reduced with instability. Dizzy older patients had higher white matter hyperintensity volumes and more theta desynchronisation during periods of instability. White matter hyperintensity volume and delta power during periods of instability were correlated, positively in controls but negatively in dizzy older patients. Delta power correlated with subjective dizziness and instability.

Conclusions:: Neural resource demands of postural control increase with age, particularly in patients with UDE, driven by small vessel disease. Compensatory postural strategies saturate in older adults with UDE, offering a neurophysiological basis to this common neurological syndrome.
SACCADES MATTER: REDUCED NEED FOR CALORIC TESTING OF COCHLEAR IMPLANT CANDIDATES BY JOINT ANALYSIS OF V-HIT GAIN AND CORRECTIVE SACCades

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Background and Aims:: Video head impulse test (v-HIT) is a quick and non-invasive test to evaluate vestibular function compared to the caloric test. The latter is, however, needed to decide on the optimal side for cochlear implantation to avoid inducing a bilateral vestibular areflexia. This study evaluates the effectiveness of using v-HIT to select cochlear implant (CI) candidates who require subsequent caloric testing before implantation.

Methods:: We used the v-HIT mean gain, MinGain_LR, the gain asymmetry (GA), and a newly defined parameter, MGS (Minimal Gain&Saccades) as models to detect the patients that would need the caloric test to decide the ear of implantation. The MGS model was defined as the MinGain_LR, except for the cases with normal gain (both sides ≥0.8) without corrective saccades. In the latter case, MGS was defined to be 1.0 (ideal gain value).
Results: The receiver operating characteristics curve showed a very good diagnostic accuracy with an area under the curve (AUC) of 0.81 for MGS. The mean gain, the minimal gain and GA had a lower diagnostic capacity; AUC of 0.70, 0.72 and 0.73, respectively. Using MGS, caloric testing could be avoided in 38 cases (a reduction of 46%), with a test sensitivity of 0.9 (i.e., missing 3 of 28 cases).
Conclusions: The newly developed model MGS balances the sensitivity and specificity of the v-HIT better than the common parameters: mean gain, MinGain_LR and GA. Therefore, considering the presence of corrective saccades in the evaluation of the v-HIT gain can considerably reduce the proportion of CI candidates requiring additional caloric testing.
ROLE OF TRANSCRANIAL MAGNETIC STIMULATION (TMS) COMBINED WITH ELECTROENCEPHALOGRAPHY (EEG) IN DISORDERS OF CONSCIOUSNESS (DOC)

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Background and Aims:: The gold standard for the differential diagnosis between unresponsive wakefulness syndrome (UWS) and minimally conscious state (MCS) is the coma recovery scale-revised (CRS-R). However, severely brain-injured patients can be unresponsive but still retain consciousness. To deal with this issue, we applied TMS-EEG as an objective brain-based tool to assess consciousness in DOC patients.

Methods:: 4 UWS and 2 MCS patients in acute and chronic stage were enrolled and underwent CRS-R and TMS-EEG recordings. Perturbational Complexity Index maximum (PCIₘₐₓ) was compared to the empirical cut-off PCI* (=0.31), which showed high sensitivity in detecting consciousness.

Results:: In chronic patients, PCIₘₐₓ values were consistent with the clinical diagnosis with >PCI* in MCS and ≤ PCI* in UWS patients. Interestingly, one UWS (PCIₘₐₓ=0.31) and one MCS (PCIₘₐₓ=0.45) patient achieved the same CRS-R score of 6, though with a different diagnosis based on visual fixation, a fluctuating clinical sign. PCI was highly sensitive to longitudinal changes, as it changed in an acute UWS patient as soon as his diagnosis rapidly upgraded to MCS.

Conclusions:: PCI confirmed the clinical diagnosis from CRS-R, providing an objective brain-based measure of consciousness, even when the behavioral responses were fluctuating or difficult to assess. Furthermore, PCI was able to longitudinally track the recovery of consciousness in an acute patient who shifted from UWS to MCS in a short time. These results are in line with previous large-scale validation studies in chronic patients, and also confirm the reliability of PCI in acute patients.
THE IMPORTANCE OF SINGLE-FIBER ELECTROMYOGRAPHY IN MYASTHENIA GRAVIS DIAGNOSIS AND PROGNOSIS: A SYSTEMATIC REVIEW

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Background and Aims: Myasthenia gravis (MG) is a serious neuromuscular impairment in the communication between nerve cells and muscles. It causes weakness in skeletal muscles, hindering their movement and control. A single-fiber electromyography (SF-EMG) is the most sensitive test for diagnosing MG. The diagnosis is confirmed with an altered SF-EMG of a clinically weak muscle. We have systematically reviewed the current application of SF-EMG techniques in the diagnosis of myasthenia gravis.

Methods: We searched PubMed to identify studies focusing on SF-EMG and its associated analytical methods in the diagnosis, prognosis and monitoring of myasthenia gravis patients.

Results: The search yielded 17 studies. Six of these were able to correlate increased SF-EMG jitter to increased severity of the disease. Mean increased jitter is a sensitive measure of severity in MG and has a potential role as a biomarker, both in terms of absolute mean jitter value or as a percentage change in those values. It does suffer in terms of specificity, though. Although SF-EMG was unable to correctly distinguish a true case of MG from a case where the patient developed Myasthenia gravis-like symptoms due to a rare mitochondrial mutation in some of the studies, SF-EMG was of primordial importance in confirming the disease when the associated AChR, striational muscle and MuSK antibodies were altogether absent from the serum.

Conclusions: Single-fiber electromyography offers significant practical and analytical flexibility compared to more invasive techniques, such as muscle biopsy. As evidenced, SF-EMG can provide the missing confirmatory link between a myriad of symptoms and MG.
Null
NEURODEGENERATION AND NEOANGIOGENESIS IN THE CEREBELLAR CORTEX IN PENTYLENETETRAZOL (PTZ)-KINDLED RATS TREATED WITH AXITINIB AND RAPAMYCIN

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Background and Aims:: Morphological changes induced in pentylenetetrazol (PTZ)-kindled rats create the basis for the resistance of chronic brain epileptization. Cerebellar contribution to kindling seizures development was shown (Godlevsky L.S.et al., 2020). To investigate histological characteristics of the cerebellar paleocortex in PTZ-kindled rats under conditions of axitinib and rapamycin administration.

Methods:: For kindling induction, we used PTZ administrations (35.0 mg/kg, i.p.) for three weeks. Axitinib (2.0 mg/kg, i.p.) and rapamycin (0.56 mg/kg, i.p.) administered during ten days. Light microscopy was performed on hematoxylin and eosin painted slices (x200 magnification). Data presented as +S.E., ANOVA Fisher test used for statistics and differences at p<0.05 are presented.

Results:: The thickness of the molecular layer decreased in kindled rats from 238.5±18.3 to 168.6±15.6 μM. The number of PC cells per 1 mm in lobule VI reduced from 65.0±2.2 to 38.0±1.5. The square of stellate cell nuclei reduced from 16.43±0.93 to 10.27±0.72 μM². The thickness of granular cells decreased from 230.2±17.7 to 156.8±13.4 μM. The density of microvessels increased in kindled rats from 25.5±2.2 to 40.7±2.8 per 2500 μM². Treatment with axitinib and rapamycin prevented kindled generalized seizure in 8 out of 11 rats. After treatment, the thickness of the molecular layer was 185.0±19.3 μM, the number of PC per 1 mm of length was 53.0±3.2 per 1 mm, the number of microvessels was 34.7±3.0, which was not different from the control (P>0.05).

Conclusions:: PTZ kindling resulted in neurodegeneration in all layers of the cerebellar cortex and increased neoangiogenesis. Treatment with axitinib and rapamycin prevented kindling-induced morphological deteriorations.
BLINK REFLEX RECOVERY CYCLE DISTINGUISHES PATIENTS WITH IDIOPATHIC NORMAL PRESSURE HYDROCEPHALUS FROM ELDERLY SUBJECTS

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Background and Aims:: The R2 component of blink reflex recovery cycle (R2BRrc) is a simple neurophysiological tool to detect the brainstem hyperexcitability commonly occurring in several neurological diseases such as Parkinson’s disease and atypical parkinsonisms. In our study, we investigated for the first time the usefulness of R2BRrc to assess brainstem excitability in patients with idiopathic Normal Pressure Hydrocephalus (iNPH) in comparison with healthy subjects.

Methods:: Eighteen iNPH patients and 25 age-matched control subjects were enrolled. R2BRrc was bilaterally evaluated at interstimulus intervals (ISIs) of 100, 150, 200, 300, 400, 500 and 750 ms in all participants. We investigated the diagnostic performance of R2BRrc in differentiating iNPH patients from control subjects using ROC analysis. Midbrain area and Magnetic Resonance Hydrocephalic Index (MRHI), an MRI biomarker for the diagnosis of iNPH, were measured on T1-weighted MR images, and correlations between R2BRrc values and MRI measurements were investigated.

Results:: Fourteen (78%) of 18 iNPH patients showed an enhanced R2BRrc at ISIs 100-150-200 ms, while no control subjects had abnormal R2BRrc. The mean amplitude of bilateral R2BRrc at the shortest ISIs (100-150-200 ms) showed high accuracy in differentiating iNPH patients from controls (AUC=0.89). R2BRrc values significantly correlated with midbrain area and MRHI values.

Conclusions:: This study represents the first evidence of brainstem hyperexcitability in iNPH patients. Given its low cost and wide availability, R2BRrc could be a useful tool for selecting elderly subjects with mild gait and urinary dysfunction who should undergo an extensive diagnostic work-up for the diagnosis of NPH.
SPINAL EXCITABILITY AND PLASTICITY IN HEREDITARY SPASTIC PARAPARESIS: A NEUROPHYSIOLOGICAL STUDY

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Background and Aims:: Pure hereditary spastic paraparesis (HSP) is a neurodegenerative disorder characterized by corticospinal pathway impairment leading to progressive lower limb weakness and spasticity. The pathophysiological role of spinal excitability and plasticity in HSP is currently unknown. This study aims to investigate spinal excitability and plasticity in HSP.

Methods:: Fifteen patients with pure HSP (SPG4) and ten controls (HS) were enrolled. Patients were clinically assessed through standardized scales (i.e., spastic paraparesis rating scale, modified Ashworth scale, Barthel scale). To examine spinal excitability, we evaluated the H reflex (HR) and reciprocal inhibition (RI) curve, at seven interstimulus intervals (ISIs), in the soleus (SO) muscle of the dominant limb. To investigate spinal plasticity, we assessed long-term changes in HR amplitude and RI curve, before and after a specific spinal cord plasticity-inducing protocol (i.e., 30-minutes of focal muscle vibration -fMV over the SO).

Results:: When considering excitability, HSP patients showed higher HR amplitude and lower HR inhibition at 2, 3 and 20 ISIs of the RI curve than HS. Concerning plasticity, HS showed significant long-term depression of the HR amplitude at 5 and 30 minutes after fMV. Conversely, in HSP patients, fMV left the HR amplitude and RI curve unchanged.

Conclusions:: HSP patients have abnormal spinal excitability (e.g., increased motoneuron excitability and decreased excitability of RI pathways). Also, the reduced modulation of the HR and RI curve following fMV demonstrates abnormal spinal plasticity. Overall, these findings suggest that abnormal spinal excitability and plasticity contribute to the pathophysiology of motor disorders in HSP.
PROLONGED DISTAL MOTOR LATENCY OF MEDIAN NERVE DOES NOT IMPROVE DIAGNOSTIC ACCURACY FOR CIDP

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Background and Aims:: Compression of the median nerve at the carpal tunnel can give demyelinating features and result in distal motor latency (DML) prolongation fulfilling the EFNS/PNS demyelinating criteria for chronic inflammatory demyelinating polyneuropathy (CIDP). Accordingly, being carpal tunnel syndrome (CTS) common in the general population, the EFNS/PNS guidelines recommend excluding the DML of the median nerve when DML prolongation may be consistent with median neuropathy at the wrist from CTS. The main aims of this study were to verify whether the inclusion of DML of the median nerve could improve electrophysiological diagnostic accuracy for CIDP and if the median nerve at the carpal tunnel (CT) was more prone to demyelination.

Methods:: We analyzed electrophysiological data from 499 patients included into the Italian CIDP Database.

Results:: According to the EFNS/PNS criteria, 352 patients had a definite, 10 a probable, and 57 a possible diagnosis of CIDP, while 80 were not-fulfilling the diagnostic criteria. The inclusion of DML prolongation of median nerve did not improve significantly the diagnostic accuracy for CIDP; overall diagnostic class changed in 6 out of 499 patients (1.2%) and electrodiagnostic class of CIDP changed from not-fulfilling to possible in only 2 patients (2.5% of not-fulfilling patients). Moreover, the median nerve at the CT was not more prone to demyelination in CIDP.

Conclusions:: Concluding, we can infer that excluding DML prolongation of median nerve does not increase the risk of missing a diagnosis of CIDP. On the other hand, importantly for clinicians, a diagnosis of CIDP based only on median DML prolongation is unlikely.
Background and Aims:: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a chronic case of polyneuropathy, commonly caused by immunological factors that attack the peripheral myelin sheath. This disease has peripheral neuropathy characteristics, predominantly motoric and symmetrical, with clinical manifestation proximal and distal weaknesses. Complications of CIDP are mostly severe motoric weakness, and respiratory failure, which is mostly found in the acute inflammatory process, is uncommon.

Methods:: Data were obtained from the medical registry in the Department of Neurology, Saiful Anwar General Hospital, Malang, Indonesia, in December 2020.

Results:: A 20-year-old woman came to ER with the chief complaint of dyspnea in the last 2 days before admission, with weakness in inferior extremities and followed by weakness in superior extremities 1 day later. There were glove and stocking paresthesia, limb ataxia, and a history of diarrhea 3 days before admission. 6 months before, patients already came with the same weakness and were diagnosed with Guillain Barre Syndrome. The patient was diagnosed with CIDP Relapse Phase, intubated in ICU, and had plasma exchange 5 times. Patient show improvement in respiratory failure but no improvement in motor power.

Conclusions:: Respiratory failure is a rare feature of CIDP complications. CIDP Relapse Phase, which presents with acute and sub-acute manifestations, resembles GBS and may require ventilator assistance because of phrenic nerve palsy involvement. Immunotherapy treatment in the form of induction and maintenance phases has been carried out in the patient, with clinical improvement results.
VisuAl evOKed pOTENTIALS (VEP) in demyelinating disease

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Background and Aims:: Optic neuritis (NO) is an acute inflammatory demyelinating disease of the optic nerve. The optic nerve's demyelination is the most common symptom found in Multiple Sclerosis (MS) and Neuromyelitis Optica (NMO). Visual Evoked Potentials (VEP) can provide additional information regarding the integrity of the anterior visual pathway from the retina to the visual cortex. Until now, VEP examination is still rarely performed, so further research is needed on the characteristics of demyelinating disease with optic neuritis.

Methods:: Data were obtained from the medical registry in the Department of Neurology, Saiful Anwar General Hospital, Malang, Indonesia, from February 2021 until March 2021.

Results:: Three cases were reported; the first patient is a patient with Secondary Progressive MS, with decreased visual acuity and bilateral optic atrophy, and VEP showed mild bilateral optic neuropathy. The second patient was a Relapse Remitting MS Patient with decreased visual acuity and bilateral optic atrophy, but the VEP results were normal. The third patient with Neuromyelitis Optica had severe visual impairment and bilateral optic atrophy, showed severe bilateral optic nerve neuropathy in VEP and RFNL thinning in Optic Coherence Tomography (OCT).

Conclusions:: VEP examination aims to determine the condition of optic neuritis in the patient. Visual disturbances can occur due to inflammatory processes, demyelination, and axonal degeneration of the visual pathways. In MS, generally, the VEP test results will show prolonged latency of P100 with normal amplitude, and in NMO with severe optic neuritis, will result in the absence of P100 in both eyes.
THE INFLUENCE OF THE ENVIRONMENT ON MOTOR MEMORY OF FIRST YEAR MEDICAL STUDENTS

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Background and Aims:: Memorizing a sequence of movements is of great importance for several human activities. We evaluated medical students motor memory in different environments.

Methods:: Twenty-four medical students from the first and 37 from the fourth year agreed to volunteer, with written approval. Half of the students from each group were tested in a calm environment: chromotherapy colors and meditation sounds. The other was in a bustling room: flashing lights and stressful sounds. They watched twice a video of 6 movements to make a surgical knot. Each volunteer was, then, asked to repeat the movements. They were recorded. The percentage of students which performed correctly each movement was calculated.

Results:: The percentages of first year medical students tested in the bustling room that made the correct movement (M) were: M1: 50%; M2: 62.5%; M3: 100%; M4: 0%; M5: 62.5% and M6: 87.5%. The percentages for volunteers in the calm environment (CE) were: M1: 81.2%; M2: 69.7%; M3: 37.5%; M4: 0%; M5: 75% and M6: 81.2%.

Conclusions:: The students performed better M1 in CE and did worse M3. We conclude that a stressful environment affects initiation of a sequence of movements, slowing the activation of neuronal circuits responsible for calling attention. The difficulty to remember correctly the third movement in CE suggests a rapid habituation of the neuronal activity. Submitting first year medical students to tests of motor memory can help to identify the “natural” skillful ones and help to plan trainings focusing on a particular step of a sequence of movements.
EEG PECULIARITIES TO HPT BY AGE AND GENDER IN PATIENTS WITH NEUROLOGICAL DISORDERS

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Background and Aims:: Introduction: Hyperventilation provocation tests (HPT) has been applied in patients for the detection of hidden disorders of the nervous system (NS) especially the pathological forms of Central NS. HPT is a relevant and useful for the study of electroencephalography (EEG). The various types of abnormal EEG response to HPT provoke different interpretation, while the research of these phenomena is still subject of investigation. The study aimed classified pathological EEG responses to HPT be age and gender of patients.

Methods:: The EEG of 985 outpatients with various functional disorders of the CNS was examined. Study classified of pathological EEG responses to hyperventilation (PERH), take into account, the age (3-6, 7-12, 13-18, 19-30, 31-50, 50<), and biological sex (mail. female) of the patients.

Results:: The disorganization of basic EEG rhythm in the first, second and third minutes of HPT shown in all age and sex groups. The all 3 types of PERH (disorganization of basic rhythm, paroxysmal discharges, epileptic activity) in the first minute were revealed in all ages, which were not observed in the second and third minutes. The all three types of PERH in the first and the second minutes were found only in women.

Conclusions:: Conclusion: We assume specificity electrical activity of the brain response to HPT depending on the time, age, and sex. PERH Shown Sex Differences, males and females are impacted differently to HPT by CNS diseases. Remember those differences play roles during examination and treatments of patients.
MEDICAL REASONING: NOT SUSTAINED ACTIVATION OF NEURONAL CIRCUITS

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Background and Aims:: For a physician, it is essential to extract relevant information from a patient’s history and identify abnormal findings of the physical examination to select exams for an accurate diagnosis. We checked the performances of medical students in different steps of the clinical reasoning.

Methods:: Twenty-five medical students that finished the first two years of basic training, gave us written approval and were tested. We presented 3 different clinical cases: colon cancer (CC), pneumonia (Pn) and stroke (St). For each case, 4 findings of the history and 2 of the examination were informed. They had to choose 2 supplementary exams. Then, we asked which other 2 exams they would require. Finally, diagnosis was required.

Results:: For CC, 52% chose the blood count and 44% a scopy as the first exams. The other exams: scopy (32%) and blood count (28%). Diagnosis: CC (36%) and lower gastrointestinal hemorrhage (12%). For Pn, 92% chose Chest X-ray or tomography and 38% blood count. Further exams were: gasometry (54%) and blood count (29%). Diagnosis: Pn (54%) and COVID-19 (33%). For St, 79% chose Head tomography and 54% blood count. The other exams: blood glucose (37.5%) and electrolytes (29%). Diagnosis: St (88%) and brain tumor (4%).

Conclusions:: Our data show that, no matter the clinical case, the students strongly disagree the second set of exams they would ask to make a diagnosis. Data from the medical consultation can activate neuronal circuits on a standardized way at an initial step of the clinical reasoning, but that activation cannot be sustained.
EFFECT OF PANDEMIC ON VISUAL MEMORY

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Background and Aims:: In pandemic era, people spend more time indoor. It is not known if their perception of the reality has changed. We decided to evaluate the visual memory of inhabitants of a city when they were exposed to outdoor pictures.

Methods:: Twenty-seven volunteers aged 25 (average) were tested. We got their written approval. They saw three pictures: P1, elements of nature, P2, elements of a city and P3, “natural” plus “human made” elements. After each picture they answered the questions: Q1: Among 3, choose one image like one you saw; Q2: Among 3, choose the image you have not seen; Q3: We asked if one element of the picture was or was not seen; Q4: We questioned if one element not present was or was not seen.

Results:: As for P1, 70% answered Q1 correctly; 81% Q2; 62% Q3 and 62% Q4. In case of P2: 44% chose the correct answer of Q1, 59% of Q2, 92% of Q3 and 62% of Q4. For P3: 59% answered correctly Q1, 62% Q2, 100% Q3 and 96% Q4.

Conclusions:: The volunteers got the best performances of Q1 and Q2, in case of P1 (70% and 81%, respectively) and the worst performances (44% and 59%) for P2. When asked if they had seen a shown object, 62% answered correctly for nature (P1). As for visual memory, our data suggest being indoor did not decrease the ability to compare elements of the nature, but did damage recall the image of an object in a non-comparative way.
MEDICAL STUDENTS' MEMORY FOR FACES: COMPARING THE INFLUENCES OF A NON-NATURAL FEATURE AND EMOTION

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Background and Aims:: The influence of emotion in the process of memorizing faces is still under discussion. We tested the medical students’ memory when they saw professional actors expressing feelings.

Methods:: Fifty-one volunteers, aged 18-30, were tested virtually. We got written approval. Twelve actors (M) and 12 actresses (F) pictures, wearing (WG) and not wearing glasses (NG) were taken: with happy (H), angry (A) and emotionless (E) faces. Ten slides containing photos of 5 actresses and 5 actors were shown. The volunteers answered 5 questions (Q1-Q5): neutral faces were presented. We asked if they were wearing or not glasses. Then, other 2 questions: to choose, among three E faces, the one wearing (Q6) and not wearing glasses (Q7).

Results:: Percentages of correct answers: Q1 (FHNG): 70%. Q2 (MHNG): 90%. Q3 (FHWG): 60%. Q4 (MANG): 92%. Q5 (MHWG): 94%. Q6 (MAWG): 57%. Q7 (MANG): 80%.

Conclusions:: The performance was greater when they saw a man, regardless his emotion and wearing or not glasses. The scores were lower if the volunteer had to choose among 3 faces. The percentage of students answering correctly which one was wearing glasses, when they saw 3 faces, was lower than when they had to choose the man not wearing it. The data suggest that to wear or not wear an accessory is more important than the facial expression for memorization in case of choosing among 3 faces. Other significant element that influences the memory for faces is gender. A non-natural feature of a face can decrease neuronal activity of the limbic system.
MULTIDIMENSIONAL ANALYSIS OF ELECTROENCEPHALOGRAPHIC TRACES

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Background and Aims:: The central nervous system can be evaluated through multiple systems of analysis, in the time domain and in the frequency domain.

Methods:: Today, all these methods allow us to take a deeper look at the organization of EEG oscillations, allowing we to expand the amount of information obtainable from the EEG traces. This also does not increase costs and does not change the low invasiveness of the EEG. Our center for many years has been oriented to carry out complex analyses of the different activities of the nervous system. The following softwares are used to perform all the analyses described: MICROMED ANALYSIS OF EEG, BQEVOQUE for the analysis of evoked potentials, NOTEPAD, LORETA SOFTWARE, DATAPLORE.

Results:: In our presentation we will present in detail the different stages of EEG signal processing

Conclusions:: We describe with detailed data clinical examples of different clinical pictures
EFFECTS OF TRANSCRANIAL ULTRASOUND STIMULATION ON TRIGEMINAL BLINK REFLEX EXCITABILITY

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Background and Aims:: Recent evidence indicates that transcranial ultrasound stimulation (TUS) modulates sensorimotor cortex excitability. However, no study has assessed possible TUS effects on the excitability of deeper brain areas, such as the brainstem. In this study, we investigated whether TUS delivered on the substantia nigra, superior colliculus, and nucleus raphe magnus modulates the excitability of trigeminal blink reflex, a reliable neurophysiological technique to assess brainstem functions in humans.

Methods:: The recovery cycle of the trigeminal blink reflex (interstimulus intervals of 250 and 500 ms) was tested before (T0), and 3 (T1) and 30 min (T2) after TUS. The effects of substantia nigra-TUS, superior colliculus-TUS, nucleus raphe magnus-TUS and sham-TUS were assessed in separate and randomized sessions.

Results:: In the superior colliculus-TUS session, the conditioned R2 area increased at T1 compared with T0, while T2 and T0 values did not differ. Results were independent of the interstimulus intervals tested and were not related to trigeminal blink reflex baseline (T0) excitability. Conversely, the conditioned R2 area was comparable at T0, T1, and T2 in the nucleus raphe magnus-TUS and substantia nigra-TUS sessions.

Conclusions:: Our findings demonstrate that the excitability of brainstem circuits, as evaluated by testing the recovery cycle of the trigeminal blink reflex, can be increased by TUS. This result may reflect the modulation of inhibitory interneurons within the superior colliculus.
STUDY OF MOTOR RESONANCE DURING MOVEMENT OBSERVATION IN PARKINSON DISEASE ASSESSED BY FUNCTIONAL NEAR-INFRARED SPECTROSCOPY (F-NIRS)-EEG CORECORDING

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Background and Aims:: In previous neurophysiological studies, mu-rhythm event-related desynchronization during observed movement, an indicator of activity in mirror neuron system (MNS), resulted impaired in Parkinson Disease (PD), even at early stages of the disease. This study tested the hypothesis of a dysfunction in MNS in PD investigating EEG activity and changes in oxy- and deoxyhaemoglobin concentration in motor cortical areas at rest and during movement observation and execution, in PD patients and healthy subjects, by EEG and fNIRS simultaneous recording.

Methods:: We enrolled 20 healthy subjects and 20 PD patients, all right-handed. Patients came from two Apulian Parkinson centers and met these inclusion criteria: age 40-80, MMSE>23, normal or corrected-to-normal visual acuity, diagnosis of Idiopathic PD at Hoehn-Yahr stage I-II. The experiment consisted of two sessions. In observation session participants observed videos in which a woman grabbed a flat or a sharp tip object and videos where the agent’s hand stopped before grabbing them. In execution session participants had to tap the space bar at the time of touch. For recording, we used 20 fNIRS channels, with probes placed on motor areas and high-density EEG with 61 scalp electrodes.

Results:: We found some differences between early PD and normal controls, with a tendency through hypermetabolism and hypersynchronization of motor cortex during coherent action observation. Detailed data about quantitative EEG analysis, oxygen metabolism and neuropsychological evaluation will be presented.

Conclusions:: Motor resonance mechanisms could compensate the abnormal motor planning in early PD, supporting specific rehabilitation strategies such as Action Observation.
Background and Aims:: Memorizing words is of great importance for physicians. The aim of this study is to explore the auditory memory of medical students through the evaluation of their ability to identify the words’ positions when said in a pre-established order.

Methods:: One hundred-twenty medical students volunteered to participate. Written approval was granted. Three different intonations of the same twelve words were recorded in equal order: neutral, happy and sad. The volunteers were separated into three subgroups (N, H and S) and answered 4 questions (Q) after hearing them. Q1 and Q2: Respectively, what was the second and eleventh word that you heard? Q3 and Q4: what was the position of the words “white” and “papaya”?

Results:: The percentages of students who answered correctly were: Subgroup H (SH): Q1: 89.2%; Q2: 62.2%; Q3: 97.3%; Q4: 86.5%. Subgroup S (SS): Q1: 83%; Q2: 56.1%; Q3: 58.4%; Q4: 78%. Subgroup N (SN): Q1: 78.6%; Q2: 54.8%; Q3: 66.7%; Q4: 73.8%.

Conclusions:: SH had a better performance remembering the word’s position, compared to SS and SN. SH and SN performed better when the word was given and the position was asked of them (Q3 and Q4), than when the position was given, and the word was asked of them (Q1 and Q2). SS had a tendency of performing better in the Q1 and Q2. For first and fourth year medical students, words in a sequence with “happier” connotations activated the memory neural circuit more than words with “sadder” connotations.
HEMISPHERIC SHIFT OF THE BRAIN ACTIVATION IN MEDICAL STUDENTS: THE ROLE OF PERIPHERAL VISION STIMULI

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Background and Aims:: Memorization of objects located in the peripheral vision field is not well known. We chose to check it in medical students from different years.

Methods:: Thirty-two first year medical students (FY), aged 18-46 (average: 23.3), and thirty-two third year medical students (TY), aged 21-43 (average: 24.8), were volunteers with written approval. They saw 3 objects at the left peripheral vision field (two of them medical ones) and 3 at the right peripheral vision field (one medical). Then, answered the question (Q): which object most called your attention?

Results:: As for FY: 59.4% chose shown objects (SO) and 31.2% not shown objects (NSO). In SO subgroup, 73.7% of the objects were on the left; 68.4% chose medical objects. As for TY: 65.6% chose SO and 18.8% NSO. In SO subgroup, 71.4% of the objects were on the left and 57.1% chose medical objects.

Conclusions:: We checked whether object position and meaning influence in peripheral vision memorization. As medical objects were better recalled, meaning is of importance. As there were medical objects in both sides and the right answers varied, position on the left was of uttermost importance. In case of non-medical objects, for FY, side was also important, but objects at right. As for TY, did not influence. Our hypothesis is that the right cerebral hemisphere is important for meaningful objects memorization. On the other hand, the left hemisphere was triggered for not meaningful objects, but its activity decreases as a medical student gets trained.
VISUAL BRAIN CORTEX ACTIVATION AND SURGICAL TRAINING

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Background and Aims:: Visual memory is essential for several professionals. We decided to check it in medical students to plan a training for future surgeons.

Methods:: Thirty-two first year medical students, average age 23.3, were volunteers. We got written approval. They answered questions (Q) of two visual memory tests. The first one: 3 objects at their left peripheral vision field (2 medical). The second test: 3 objects at the right peripheral vision field (one medical). The questions were about: Q1: All seen objects; Q2: Meaningful object; Q3: Objects seen on the right; Q4: Objects seen on the left; and Q5: the lower right position object.

Results:: As for Q2: 59.4% chose shown objects (SO). Among them, 52.6% chose objects located in an intermediate position, 31.6% in the upper and 15.8% in the lower position; 73.7% on the left, 26.3% on the right. In case of Q5: 18.8% chose the correct object (mask), 75% told they did not remember.

Conclusions:: Parameters as side, meaning and position of an object may influence the peripheral vision memorization of objects. Brain activation of the visual areas of first year medical students was greater when they saw objects in an intermediate position, secondly in a high position. This finding is of importance to plan surgical trainings.
ACTIVATION OF NEURONAL CIRCUITS AND MANIPULATION OF THE PERIPHERAL VISION: A TOOL FOR MEDICAL TRAINING

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Background and Aims:: The peripheral vision (VP) field is favorable for the identification of scenes. To improve memorization of VP objects can be useful to train future surgeons. We checked medical students’ ability to pay attention in peripheral elements.

Methods:: Thirty-two first year medical students were volunteers for an online test. We got written approval. They stayed between 15 and 25 centimeters from the screen, so that the objects would be in their VP fields. The tests were recorded. We asked the students to focus a central marker. Three different thematic sequences: T1 (black and white), T2 (medical) and T3 (colorful) with 4 scenes each. There was a progressive increase in the number of elements. After each scene they answered the question (Q): among 3 options which did you see?

Results:: For T1, the percentages of students who answered correctly were 71.9% (Q1); 37.5% (Q2); 31.3% (Q3) and 28.1% (Q4). For T2, they were 65.6% (Q1); 59.4% (Q2); 9.4% (Q3) and 18.1% (Q4). For T3, the percentages were 87.5% (Q1); 34.4% (Q2); 34.4% (Q3) and 56.3% (Q4).

Conclusions:: In case of a low number of elements, the performance was greater for T3. When there was a slight increase in quantity, the highest score was for T2. Nevertheless, there was a significant decrease in that score with an even greater number. Considering the final scenes, again, the performance was the highest for T3, but very low for T2. The increase of colored elements activates neuronal circuits related to the excitation of the cones, in a reverberating way.
INFLUENCE OF EMOTIONS IN MEDICAL STUDENTS: FOCUSING ON THE MEMORY OF RECOGNITION OF WORDS

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Background and Aims:: The relation between auditory memory and emotions needs to be further explored. The aim of this study is to explore the auditory memory of medical students through the evaluation of their ability to recognize words that were said from words that were not said.

Methods:: One hundred-twenty medical students volunteered to participate. Written approval was granted. Three different intonations of the same twelve words were recorded in equal order: neutral, happy and sad. The volunteers were separated into three subgroups (N, H and S) and answered 8 questions (Q) after hearing them. Q1-Q4: among the 3 words, which word did you hear? Q5-Q8: among the 3 words, which word did you not hear?

Results:: The percentages of students who answered correctly were: Subgroup H: Q1: 100%; Q2: 100%; Q3: 97.3%; Q4: 94.6%. Q5: 94.6%; Q6: 94.6%; Q7: 97.3%; Q8: 97.3%.Subgroup S: Q1: 100%; Q2: 92.7%; Q3: 92.6%; Q4: 97.6%; Q5: 90.2%; Q6: 97.6%; Q7: 92.7%; Q8: 100%. Subgroup N: Q1: 97.6%; Q2: 100%; Q3: 90.5%; Q4: 97.6%; Q5: 95.2%; Q6: 95.2%; Q7: 95.2%; Q8: 95.2%.

Conclusions:: Considering the ability of remembering words that were or were not said, there were more than 90% of correct responses for all intonations. SH and SN performed better with words that were said than the words that were not said. SS had a tendency to perform better with words that were said. Our hypothesis is that activation of auditory neuronal circuits and of the limbic system depends on the emotion perceived by the listener.
THE INFLUENCE OF THE ENVIRONMENT ON MOTOR MEMORY OF FOURTH YEAR MEDICAL STUDENTS

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Background and Aims:: Motor memory is essential in medical education. To evaluate the influence of the environment in motor memory, we tested the surgical skills on fourth year students in different sets.

Methods:: Twenty-four medical students from the first and 37 from the fourth year agreed to volunteer, with written approval. Half of the students from each group were tested in a calm environment: chromotherapy colors and meditation sounds. The other was in a bustling room: flashing lights and stressful sounds. They watched twice a video of 6 movements to make a surgical knot. Each volunteer was, then, asked to repeat the movements. They were recorded. The percentage of students which performed correctly each movement was calculated.

Results:: The percentages of fourth year medical students tested in the bustling room that made the correct movement (M) were: M1: 82.4%; M2: 70.6%; M3: 52.9%; M4: 28.6%; M5: 47.1% and M6: 94.1%. The percentages for volunteers in the calm environment (CE) were: M1: 95%; M2: 80%; M3: 65%; M4: 20%; M5: 75% and M6: 85%.

Conclusions:: The environment significantly influences the performance of motor memory, demonstrated by better performance in CE. Regardless the environment, movement 4 was difficult to be made. Scores were higher in first 3 and last 2 movements, demonstrating that performing motor tasks in a sequence, at a certain step, a habituation occurs. Submitting fourth-year students to motor memory tests highlights the importance of skills training for future surgeons, which facilitates motor learning.
RELATION BETWEEN VISUAL AND AUDITORY NEURONAL CIRCUITS ACTIVATION: ITS INFLUENCE ON THE LIMBIC SYSTEM

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Background and Aims:: It is important to compare the memory of medical students for scientific knowledge. For that, we used a test of visual memorization and concentration with music to evoke feelings.

Methods:: Forty-eight first and third medical students were volunteers. We got written approval. We showed Slide 1 with 2 objects from each of the categories: kitchen, school and medical, in 6 different action neutral scenes (one object per scene). Slide 2: the objects were in scaring scenes. While seeing the first slide they listened to a “calm and happy” music. As for the second slide they listened to a “sad and fearful” music. After that, the volunteers answered the questions (Q) 1: Which objects did you see on slide 1? and Q2: Which objects did you see on slide 2? Q3: Do you think the music on slide 1 correlates with the images? Q4: Do you think the music on slide 2 correlates with the images?

Results:: The percentages of students that remembered all objects (4) were: for Q1, 43.8% and for Q2, 58%. In case of Q3: 50% answered “yes” and 50% answered “no”. Q4: 66.7% answered “yes” and 33.3% answered “no”.

Conclusions:: The ability of remembering an object in a scaring scene listening to a fearful music was greater than the one in a neutral scene. However, the difference was not as significant as one might expect. When a high percentage of volunteers found a correlation between the emotions related to the music and the scenes, their working memory was better.
DIFFERENTIATING MULTIFOCAL ACQUIRED DEMYELINATING SENSORY AND MOTOR NEUROPATHY (MADSAM) WITHOUT SENSORY LOSS FROM MULTIFOCAL MOTOR NEUROPATHY (MMN): A CASE STUDY

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Background and Aims:: MADSAM is a CIDP variant where patients present with asymmetrical motor weakness in distal limbs with sensory symptoms and signs. The differentiation of MADSAM from MMN can be challenging when there is lack of sensory involvement in the former. We report a case of MADSAM without sensory signs or symptoms, which was differentiated from MMN using SSEP.

Methods:: A 48-year-old man presented with asymmetric, gradual onset distal lower limb weakness which progressed to involve distal upper limbs after one and a half years. His sensory system examination was normal.

Results:: The NCS showed motor conduction blocks in clinically affected nerve segments with normal sensory conduction. The CSF analysis revealed elevated proteins at 57mg/dl with no cells. Due to the suspicion of a CIDP variant, SSEPs were performed. SSEPs of the affected segments were delayed confirming proximal sensory involvement. The diagnosis was made as MADSAM. Patient was treated with intravenous immunoglobulin followed by long-term oral prednisolone. He responded to treatment with evidence of clinical and neurophysiological improvement in the previously affected nerve segments at 10 months follow up.

Conclusions:: MADSAM with pure motor symptoms and motor predominate neurophysiological findings, can be misdiagnosed as MMN. Therefore, CSF analysis and recording of SSEPs are mandatory.
INTRAOPERATIVE MAPPING AND MONITORING OF THE OPTIC PATHWAY

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Background and Aims:: The identification of the visual pathway during surgery for tumours in visual areas is challenging. We present our experience in visual pathway mapping and monitoring, describing the role of direct mapping of the optic radiations and different techniques of VEPs monitoring, employing both Scalp Recording (SR) and the use of strip electrode positioned over the primary visual cortex for Direct Cortical Recording (DCR).

Methods:: Single-centre prospective cohort study of patients admitted for surgery of intra-axial visual eloquent lesions. Pre-operative mapping – tractography – and intraoperative monitoring (surface – SR - and direct cortical recordings - DCR) and mapping (subcortical stimulation) data were collected along with demographic and clinical information and correlated with extent of resection, surgical technique and visual outcome

Results:: 34 patients were included (20 males, 14 females; mean age of 54.91±2.81 years). 19 (55.88%) patients had homonymous quadrantanopia or hemianopia. Occipital and Parietal location had the larger extent of resection – GTR in 91.67% and 84.62%, respectively, p=0.023 - and the occipital location was related with the better visual outcome - 83.33% patients remained stable and 15.38% improved (p=0.006). DCR was predominantly used in occipital lesions (p=0.002), SR in temporal and parietal lesions (p<0.0001) and positive subcortical stimulation was achieved in parietal and occipital lesions (p=0.007). The DCR was better in metastasis than in gliomas (p=0.040) and was related with the visual outcome (p=0.019).

Conclusions:: Direct cortical recording of VEPs and subcortical stimulation of the optic radiations are reliable techniques to monitor and map the visual pathways in asleep patients.
Background and Aims: The peripheral vision (VP) field is favorable for the identification of scenes. We checked medical students’ ability to pay attention in peripheral elements.

Methods: Fifty-two medical students (first [G1] and third years [G2]) were volunteers for an online test. We got written approval. They stayed between 15 and 25 centimeters from the screen, so that the objects would be in their VP fields. The tests were recorded. The students had to focus a central marker. Three different thematic sequences: T1 (black and white), T2 (medical) and T3 (colorful) with 4 scenes each. There was a progressive increase in the number of elements. After each scene they answered the question (Q): among 3 options which did you see?

Results: G1 for T1, the percentages of students who answered correctly were 71.9% (Q1); 37.5% (Q2); 31.3% (Q3) and 28.1% (Q4). For G2, they were 70% (Q1); 45% (Q2); 20% (Q3) and 25% (Q4). G1 for T2, 65.6% (Q1); 59.4% (Q2); 9.4% (Q3) and 18.1% (Q4). For G2, they were 75% (Q1); 60% (Q2); 15% (Q3) and 50% (Q4). G1 for T3, the percentages were 87.5% (Q1); 34.4% (Q2); 34.4% (Q3) and 56.3% (Q4). For G2, they were 95% (Q1); 55% (Q2); 50% (Q3) and 60% (Q4).

Conclusions: The G2 had better results when medical elements were shown. In the other themes, this advantage was lower. However, there are similar curves of variation in both groups. The longer the period of training, the easier was the ability to recall a seen element.
Background and Aims:: Visuospatial and association skills are of great importance for human relationship. In pandemic times we do not know if and how much they have been damaged. We propose an easy method to check them. Inhabitants of a big city were tested.

Methods:: Twenty-seven volunteers aged 25 (on average) had their visuospatial and association skills tested. All of them gave us a written approval. They saw three pictures: P1: natural objects, P2: human-made objects and P3: both kinds. After each scene they had to choose a professional they would include in the seen picture. The options were: a garbage collector, a physician, a teacher, a musician, and a delivery biker. It was possible to choose more than one.

Results:: As for P1, 55% chose the inclusion of a garbage collector and the same percentage would choose a musician. In case of the picture of the city (P2), 74% would include a delivery biker. For the mixed scene (P3), 48% would include a garbage collector and 48% a delivery biker.

Conclusions:: Half of the volunteers were worried about cleaning and the same percentage was interested in a musician when they saw natural objects. Three fourths chose a delivery worker when they saw human-made objects. The data suggest that staying indoors too long called much attention to cleaning (even in scenes with no garbage) and to pleasant activity (in a nature scene but not in a street scene). The activation of neuronal circuits important for association between visual stimuli and their meanings seems to be impaired.
Background and Aims:: The amnestic type of mild cognitive impairment (aMCI) carries an increased risk of conversion to Alzheimer disease (AD) and therefore its early identification is relevant for the development of disease-modifying treatments. Considering non-invasive simple diagnostic methods, we focused on visual evoked potentials (VEPs) as putative biomarker of cholinergic disfunction. We thus studied patients with MCI and AD by means of paired-pulse flash-visual evoked potentials (paired-F-VEPs). This technique, recently revived, analyses the overall excitability of visual system as detected from the cortical occipital signal.

Methods:: We enrolled 12 adult patients with aMCI and 12 with AD. Fourteen normal subjects of similar age and sex acted as controls. Stimuli were single flashes, intermingled at random to flash pairs at critical interstimulus intervals (ISIs, 16.5 to 125ms) with closed eyes. The “single” (unconditioned) F-VEP was split into a “main complex” (50 to 200ms after the flash) and a “late response” (200 to 400ms). As for paired stimulation, the “test” F-VEP emerged from electronic subtraction of the “single” F-VEP to the “paired” F-VEP. Its size was expressed as “test”/”single” F-VEP*100.

Results:: Patients with aMCI did not show the size reduction (at ISIs 50 and 62.5ms) which was typical among both the controls and AD (p<0.016), when the “late response” was considered. No changes of the “main complex” were detected.

Conclusions:: Paired-F-VEPs document a defective neural inhibition in the visual system of patients with aMCI. Paired-F-VEPs may warrant inclusion in future clinical studies, to evaluate its potential role in the pathophysiology and management of aMCI.
CONTRIBUTION OF DIFFERENT SOMATOSENSORY AFFERENT INPUT TO SUBCORTICAL SOMATOSENSORY EVOKED POTENTIALS IN HUMANS

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Background and Aims:: Cortical projection of the somatosensory fibers of different modalities has been studied in humans. The aim of this study was to investigate the subcortical somatosensory evoked potentials (SEPs) to electrical stimulation of either muscle or cutaneous afferents.

Methods:: SEPs were recorded in 6 patients suffering from Parkinson’s disease who underwent electrode implantation in the pedunculopontine (PPTg) nucleus area. We compared SEPs recorded from the scalp and from the intracranial electrode contacts to electrical stimuli applied to: 1) median nerve at the wrist, 2) abductor pollicis brevis motor point, and 3) distal phalanx of the thumb. Also the high-frequency oscillations (HFOs) were analysed.

Results:: After median nerve and pure cutaneous (distant phalanx of the thumb) stimulation, a P1-N1 complex was recorded by the intracranial lead, while the scalp electrodes recorded the short-latency far-field responses (P14 and N18). On the contrary, motor point stimulation did not evoke any low-frequency component in the PPTg traces, nor the N18 potential on the scalp. HFOs were recorded to stimulation of all modalities by the PPTg electrode contacts.

Conclusions:: Our study showed that: a) the scalp N18 wave can be evoked by the cutaneous input, while the pure stimulation of the muscular afferents does not evoke it; b) both presynaptic and postsynaptic HFOs can be recorded at level of the cuneate nucleus after all stimulation modalities. These results suggest that the stimulus processing within the cuneate nucleus depends on modality, since the reverberation mechanism producing the scalp N18 potential is triggered only by the cutaneous but not the muscular input.
ENVIRONMENTAL TRIGGERING EMOTIONS: ENHANCING MEDICAL STUDENTS VISUAL MEMORY

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Background and Aims:: Memorization of details of a scene depends on different brain neuronal circuits. We decided to study how emotions influence visual memories.

Methods:: Fifty-one third year medical students were selected (21 to 30 years) and divided into two groups: with emotion (WE: 23) and with no emotion (NE: 28). They were in two classrooms. Four images were projected: a bedroom, a classroom, an operating room, and a kitchen. Then they had to answer four questions (Q) after each image: the color of the wall (Q1,5,9,13), which object they saw (Q2,6,10,14), which object was not in the scene (Q3,4,7,8,15,16). In the room where were NE students they saw the pictures and listened to no music. In the other room (WE): four musics were played with each image, respectively: happy, angry, sad, and relaxing ones.

Results:: In the NE: 75% got right answers for Q1 and 89% for Q3, 86% for Q6, Q9 and Q12. For WE: 61% got right answers for Q1 and 66% for Q3, 66% for Q6, 100% Q9 and 96% Q12.

Conclusions:: Students in a non-medical (NM) emotional environment had lower performance memorizing details of a scene. However, in case of the medical (M) environment emotion facilitated memorization. In a NM neutral environment volunteers got higher scores memorizing objects than color. On the other hand, in M those scores were similar and higher. Our data support that visual memory neuronal circuits were overactivated by the combination of long term stored emotions (the vision of an operating room) and present emotions (musics).
Background and Aims:: To evaluate serum antidiuretic hormone (ADH) its receptors and renin levels in Cerebral salt wasting (CSW) in tuberculous meningitis (TBM).

Methods:: Patients diagnosed with definite (n=30) or probable TBM (n=47) who developed hyponatremia (CSW, SIADH or miscellaneous causes) were included. Sequential measurement of Serum ADH, ADH-R and renin activity by enzyme linked immunosorbent assay was done and correlated with serum sodium level, urinary output and fluid balance

Results:: Out of 79 TBM patients, CSW was observed in 36, SIADH in four and miscellaneous hyponatremia in eight patients. CSW patients had a longer hospital stay (P<0.001), lower GCS score (P<0.007), higher MRC grade (P<0.007) and a lower serum Na (P<0.001) compared to non-CSW TBM patients. In severe CSW patients, Serum ADH and ADH-R were correlated with hyponatremia and returned to baseline on correction, however, serum renin levels remained elevated. Serum ADH was related to hyponatremia but ADH-R and renin were not. ADH -R and renin levels did not significantly differ in CSW and SIADH

Conclusions:: CSW is the commonest cause of hyponatremia in TBM, and correlates with disease severity. ADH is related to hyponatremia, but ADH receptor and renin are not
UNCLASSIFIED SUBTYPE OF GUILLAIN-BARRÉ SYNDROME IS ASSOCIATED WITH QUICK RECOVERY

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Background and Aims:: Electrophysiological classification of Guillain-Barré syndrome (GBS) is important for predicting its clinical course. However, few reports discuss GBS patients who do not fit into the acute inflammatory demyelinating polyneuropathy (AIDP) or acute motor axonal neuropathy (AMAN) classifications of GBS. Therefore, the present study focused on the features of unclassified types of GBS and compared these to AIDP and AMAN.

Methods:: We compared clinical symptoms, nerve conduction, and laboratory data among patients with AIDP, AMAN, and unclassified subtypes of GBS, according to criteria developed by Rajabally, Hadden, and Ho.

Results:: According to the Rajabally criteria, the F wave frequency of the upper and lower extremities in the unclassified subgroup was higher than that of AIDP and AMAN. However, according to the Hadden and Ho criteria, the frequency of the F wave in only lower extremities in the unclassified subgroup was higher than that in other subgroups. The unclassified subgroups showed better prognosis using the Rajabally criteria.

Conclusions:: Classification with the Rajabally criteria is a useful tool for predicting prognosis and determining treatment in patients with GBS, and unclassified patients exhibit quick recovery.
DISTINCT NEURONAL CIRCUITS TO MEMORIZE FACES: MODULATION OF THE LIMBIC SYSTEM

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Background and Aims:: Memorizing faces is especially important for physicians. We analyzed the effect of gender-linked features and emotion for that memorization in medical students.

Methods:: Fifty-one students, aged 18-30 were tested online, with written approval. Pictures from 12 actors (M) and 12 actresses (F) were taken: with happy (H), angry (A) and emotionless (E) faces. The men were with (Mu) and without a mustache (wMu) and the women using (uL) or not using lipstick (nL). We showed ten slides of 5 actresses and 5 actors, wearing or not accessories. They answered 6 questions (Q1-Q6): in each, an E face. We asked if they were wearing mustache or using lipstick. Other questions, to choose among three E faces, the one using lipstick (Q7) and the one not wearing mustache (Q8).

Results:: Percentages of correct answers: Q1 (FAuL): 78%, Q2 (MHwMu): 39%, Q3 (FHnL): 54%, Q4 (FAnL): 86%, Q5 (MHMu): 67%, Q6 (FHuL): 84%, Q7 (FEuL): 49%, Q8 (MAwMu): 74%.

Conclusions:: After the students saw faces with gender-linked accessories (mustache and lipstick) it was easier to remember female’s faces (Q4 and Q6). The performance of the volunteers was greater when they saw angry faces, no matter the gender or the presence of accessories (Q1, Q4 and Q8). Male or female’s happy faces were easier to be recalled when they were with accessories (Q2, Q3, Q5 and Q6). Our data strongly suggest that gender, emotion, and accessories affect the memorization for faces in specific ways. Therefore, the neuronal circuits important for that kind of memory are distinct.
WHOLE PLANTAR NERVE CONDUCTION STUDY: AN USEFUL TOOL IN DIAGNOSIS OF DIABETIC POLYNEUROPATHY

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Background and Aims:: Whole plantar nerve (WPN) allows the registration of a summation sensory action nerve potentials (SNAPs), simultaneously recording from both lateral and medial plantar nerves. Thus, WPN may be useful in length-dependent polyneuropathy, as well as diabetic peripheral neuropathy. We aimed to assess the reliability of whole plantar nerve (WPN) conduction study in diabetic subjects.

Methods:: This single-center prospective observational case-control study involved 70 type II diabetes mellitus patients and 62 healthy controls referred to I Division of Neurology of the University of Campania “Luigi Vanvitelli” between October 2019/October 2020. All subjects performed validated screening tests of neuropathy, nerve conduction study (NCS) of the sural nerve, WPN and sympathetic skin response (SSR).

Results:: Median SNAPs amplitude (2.10µV vs 4.9µV, p=0.001) and sensory conduction velocity (SCV) (40µV vs 42.7µV, p=0.013) recorded by WPN were significantly lower in type II diabetes mellitus patients. Likewise, proximal sural nerve conduction revealed that both SNAPs amplitude (6.4 [3.48 – 12.4] µV vs 11.25 [6.2 – 16.7] µV, p=0.001) and SCV (50.1 [45.68 – 54.9] m/s vs 53.6 [49 – 57.6] m/s, p=0.006) were significantly lower in the diabetic group, as compared to HC.

Conclusions:: Our data support WPN conduction study reliability in characterizing lower limbs’ most distal sensory nerve fibers. Thus, WPN may represent a useful tool for diabetic PN studies.
PRECLINICAL MARKERS OF NEUROPATHIC DAMAGE IN TYPE 1 DIABETES MELLITUS

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Background and Aims:: Diabetic neuropathy (DN) is the most common neurological complication of diabetes mellitus (DM). Although DN has been related to long-lasting disease, early signs might be appreciable after a few years from DM onset. Our study aimed to detect with clinical and multimodal neurophysiological tests the presence of DN in a group of patients with DM type 1.

Methods:: Fifty-six patients affected by DM type 1 attending the Metabolic Disease Unit of Magna Graecia University of Catanzaro underwent to clinical screening for DN through Michigan neuropathy screening instrument (MNSI) and multimodal neurophysiological tests including electroneurography, laser evoked potentials and neurovegetative function tests (skin sympathetic response and evaluation of heart rate variation).

Results:: Among 56 patients with mean age of 41±15 and disease duration of 20±11, 42.8% had symptoms and 51.8% had clinical signs of DN. Neurophysiological tests showed that 82.2% presented a DN: 19.6% have only large fiber neuropathy, manifesting mainly with demyelinating and/or axonal length-dependent polyneuropathy or entrapment neuropathy; 17.6% had only small fiber neuropathy; whereas 44.6% had both small and large fibers involvement. About a third of patients with DN resulted negative for MNSI test. Comparison with demographic data and continuous glucose monitoring parameters revealed a significant association between presence of DN with or without clinical sign and symptoms and age, disease duration and time below range.

Conclusions:: this study showed that multimodal neurophysiological tests are more sensitive to identify DN than traditional clinical tests. Further studies are needed to investigate the relationship between DN and continuous glucose monitoring parameters.
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PUPIL SIZE IS INFLUENCED BY TRANSCUTANEOUS VAGAL NERVE STIMULATION UNDER SPECIFIC STIMULATION INTENSITY AND ILLUMINANCE CONDITION

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Background and Aims:: Pupil size has gained attention as a promising biomarker of vagal activation in different studies on animal models. Locus Coeruleus (LC) is the main noradrenergic nucleus of the central nervous system and plays a key role in regulating pupil diameter. Transcutaneous vagal nerve stimulation (taVNS) is a non-invasive technique used to stimulate cutaneous auricular afferent branch of the vagus nerve at the external ear. Cervical taVNS is a currently approved treatment for primary headache. However, taVNS mechanisms of action are still not known even if animal studies have reported a potential effect of taVNS on LC. Our aim was to investigate the effects of taVNS on pupil diameter in healthy subjects.

Methods:: All subjects (n = 12) received taVNS at the left external acoustic meatus and control stimulation at the left earlobe during the same experimental session. Different intensities and illuminance conditions (scotopic, mesopic, photopic) for both conditions were tested.

Results:: In scotopic illuminance condition real taVNS at 2 mA was capable of inducing a larger pupil dilatation, in comparison to baseline and 2 mA control stimulation.

Conclusions:: Our study demonstrates that taVNS induces pupil dilation under specific illuminance condition and at a specific stimulation intensity. Pupil dilation during taVNS could be used as an online and easy-to-use indicator of the effectiveness of the stimulation, in order to optimize therapeutic applications of this technique, also in neurodegenerative diseases in which the activity of the LC-noradrenergic network is supposed to play a role in the pathogenesis.
POSTSYNAPTIC NEUROMUSCULAR JUNCTION DEFECT IN A PATIENT WITH MILLER FISHER SYNDROME

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Background and Aims:: Miller Fisher syndrome (MFS) is an acute immune-mediated neuropathy. To date only few studies reported a possible overlap of Myasthenia Gravis (MG) and MFS in patients with acute ophthalmoplegia. We report the case of a patient diagnosed as MFS with a coextistent neuromuscular junction defect.

Methods:: A 77-year-old Chinese female, without significant previous neurological history, presented in our Emergency Department with acute ophthalmoplegia after recent fever and faringodinia. Neurological examination revealed clinical signs (areflexia, complete ophthalmoplegia and ataxia) consistent for MFS.

Results:: Instrumental tests (neuroimaging, CSF, nerve conduction studies, serum antibodies tests) were performed and the patient was diagnosed with MFS. Repetitive nerve stimulation also showed coextistent significant decremental motor response suggesting an overlapping postsynaptic neuromuscular transmission defect. Patient underwent plasmapheresis with a progressive improvement until full clinical recovery.

Conclusions:: Although the overlap of MG and MFS is very rare, it should be considered in the differential diagnosis in neuro-ophthalmic diseases. Our findings emphasize the importance of electrophysiologic tests for neuromuscular transmission also in MFS in order to build a spectrum of clinical, serological and electrodiagnostic characteristics and better understand the mechanisms that determine ophthalmoplegia and the treatment response. We encourage other studies to collect further related data.
PATIENTS WITH UNRESPONSIVE WAKEFULNESS SYNDROME PRODUCE HIGH-AMPLITUDE AUDITORY STEADY-STATE RESPONSE

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Background and Aims: The unresponsive wakefulness syndrome (UWS) is one of the unfavorable states that are characterized by a condition of arousal without signs of awareness. Most UWS patients are unresponsive to external stimuli. However, they often open their eyes and are capable of swallowing. In addition, most cases preserve their sleep-wake cycles. These symptoms make it difficult to understand the symptom. The author studied the electrophysiological response of UWS patients, and found a unique means to describe the syndrome.

Methods: Ten cases with UWS were studied. I examined their electroencephalogram (EEG), auditory brainstem response (ABR) and auditory steady-state responses (ASR) simultaneously. Ally ASR data set were processed by the fast Fourier transformation method, and a power spectrum around the 40 Hz-frequency band was calculated. These records were compared to the data obtained from normal volunteers.

Results: All patients exhibited low-voltage EEG less responsiveness to external stimuli. In contrast, they showed a significantly high-amplitude ASR. Waveforms and each peak’s latency of their ABR records were almost normal. These findings suggested deteriorated cerebral function and preserved brainstem activity. The ASR records may indicate dysfunction of cerebral inhibition system in the neural activity of the brainstem reticular formation.

Conclusions: Findings from the electrophysiological examinations revealed cerebral hypofunction and preservation of brainstem activity. In addition, the results of the ASR examination suggested malfunction of the cortical inhibitory system against brainstem neural activity. This result is thought to be a unique feature in the UWS patients and may help to understand the pathophysiology of UWS.
OVERT AND COVERT EFFECTS OF COGNITIVE FATIGUE ON ATTENTION NETWORKS

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Background and Aims:: Cognitive fatigue refers to a variation of the psychophysiological state during or after prolonged periods of mental activity that requires work efficiency, and could lead to temporary deterioration of attentional functioning, especially top-down attention and cognitive control. The present study aims to verify the effects of cognitive fatigue on attention in the context of the three attentional networks described by Posner, by using behavioral and psychophysiological measures, to detect variations in overt and covert responses respectively.

Methods:: Thirty young healthy subjects were enrolled in the study, 15 in the “fatigue” and 15 in the control group. Cognitive fatigue was provoked by a continuous arithmetic task lasting 1 hour, and the EEG recordings were conducted before and after the task, while subjects were performing the attention network test. The N1, N2 and P3 components were analyzed for the alerting, orienting and conflict networks, in conformity with behavioral analysis.

Results:: No difference emerged between groups in networks’ efficiency scores and in N1 and P3 amplitudes related to the alerting network. As regards the orienting network, P3 amplitude was significantly reduced in the fatigue group alone (p=0.02), while no differences emerged in N1 amplitude. As regards the conflict network, both N2 and P3 amplitudes were significantly reduced in the fatigue group alone and selectively for the incongruent target (p<0.001; p=0.001 respectively).

Conclusions:: Our results suggest that, in young healthy subjects, cognitive fatigue interferes with goal-driven attention especially when the task demand is higher, sparing the bottom-up attention control mechanisms and in absence of any overt observable effect.
CEREBELLUM IN TIMING CONTROL: EVIDENCE FROM CONTINGENT NEGATIVE VARIATION AFTER CEREBELLAR TDCS.

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Background and Aims: Timing control is defined as the ability to quantify time. The temporal estimation of supra-seconds range is generally seen as a conscious cognitive process, while the sub-seconds range is a more automatic cognitive process. It is accepted that cerebellum contributes to temporal processing, but its function is still debated. The aim of this research was to better explore the role of cerebellum in timing control. We transitorily inhibited cerebellar activity and studied the effects on CNV components in healthy subjects.

Methods: Sixteen healthy subjects underwent a S1-S2 duration discrimination motor task, prior and after cathodal and sham cerebellar tDCS, in two separate sessions. In S1-S2 task they had to judge whether the duration of a probe interval trial was shorter (Short-ISI-trial:800ms), longer (long-ISI-trail:1600ms), or equal to the Target interval of 1200ms. For each interval trial for both tDCS sessions, we measured: total and W2-CNV areas, the RTs of correct responses and the absolute number of errors prior and after tDCS.

Results: After cathodal tDCS a significant reduction in total-CNV and W2-CNV amplitudes selectively emerged for Short (p<0.001; p=0.003 respectively) and Target-ISI-trial (total-CNV: p<0.001; W2-CNV:p=0.003); similarly, a significant higher number of errors emerged for Short (p=0.004) and Target-ISI-trial (p=0.07) alone. No differences were detected for Longer-ISI-trials and after sham stimulation.

Conclusions: These data indicate that cerebellar inhibition selectively altered the ability to make time estimations for second and sub-second intervals. We speculate that cerebellum regulates the attentional mechanisms of automatic timing control by making predictions of interval timing.
INTRAOPERATIVE NEUROPHYSIOLOGICAL MONITORING URGENT SYMPTOMATIC EXTRAĆTRANIAL INTERNAL CAROTID ARTERY DESOBLITERATION.

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Background and Aims:: Background: Surgical recanalization extracranial internal carotid artery (ICA) occlusion is an off-label acute stroke therapy because of conflicting results. Common carotid artery (CCA) cross-clamp might be the main cause of intraoperative ipsilateral stroke and unacceptably high rate of poor outcome. Intraoperative median somatosensory evoked potentials (SEP) monitoring is an established tool for selective shunting and intraoperative stroke prevention. Aim: Rate of necessary interventions induced by intraoperative SEP changes during urgent ICA recanalization.

Methods:: Acute ischemic stroke with extracranial ICA occlusion within 24 hours from last seen normal with no contraindications for urgent recanalization therapy. Prospectively recruited 33 patients, 30 males (90.1 %), average age 70.4 ± 8.9 years (52-88). Symptomatic side on left in 22 (66.7%), NIHSS median 6.0, interquartile ratio (2.0-12.0). Prestroke modified Rankin scale (mRS) 0, 1 and 2 were in 30 (91.9 %), 1 and 2, respectively.

Results:: Recanalization was achieved in 32 (96.7%). SEP amplitude dropped after CCA crossclamp in 6 patients (18.2%). SEP recovered after mean arterial pressure increase >100 mmHg, shunt insertion and final flow restoration in 3, 2 and 1 patient, respectively. Surgical complications were in 6 (18.2%) patients. Four haematomas were resolved after urgent surgical revision. Four ipsilateral cranial nerve lesions recovered spontaneously within 3 months. 3month mRS-3M 0-1, 2, 4-5 and 6 were 23 (69.7%), 5, 2 and 3, respectively. Overall permanent morbidity and mortality was 5 (15.2%).

Conclusions:: Intraoperative SEP during urgent ICA desobliteration seems to be valuable because of intraoperative brain ischemia prevention and permanent morbidity and mortality reduction.
A NEW, SENSITIVE BIOMARKER FOR ABNORMAL CORTICAL EXCITABILITY: SINGLE TRIAL BASED SYNCHRONIZATION AND DESYNCHRONIZATION WITH CORTICAL MYOCLONUS

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Background and Aims:: Giant somatosensory evoked potentials (SEPs), i.e., enlarged cortical components of SEPs, represent abnormal cortical excitability such as cortical myoclonus (CM). Recently, we reported high-frequency oscillations (HFOs) with a part of giant SEPs specifically observed in benign adult familial myoclonus epilepsy (Tojima et al., 2021). However, no clear HFOs after N33 were observed. We herein hypothesized, in CM patients, late cortical abnormal excitability may be poorly synchronized in average method and thus only detectable by single trial, event-related synchronization (ERS) and desynchronization (ERD). We also compared ERS/ERD between CM patients and healthy controls (HCs).

Methods:: This retrospective study included patients from 2017 to 2020 showing CM and giant SEPs to median nerve stimulation, and all single-trace data were available. We investigated time-frequency analysis using single-trace data and defined significant power increase and decrease compared to baseline activities as ERS/ERD. Occurrence rates of ERS/ERD in CM patients and those in SEP of age-matched HCs were compared.

Results:: In 46 giant SEPs to one arm in 23 patients and 33 SEPs in 17 HCs, ERS/ERD up to 1000Hz were observed between 20-150ms commonly. Occurrence rate of ERS (83% vs. 30%, p<0.01) and ERD (59% vs. 15%, p<0.01) was significantly higher in CM patients.

Conclusions:: Time-frequency analysis of single-trace data revealed ERS/ERD after N33 in CM patients. It indicates that oscillatory activity was totally obscured in the background of averaged SEP. It could be a new sensitive biomarker for abnormal cortical excitability of CM, beyond “averaged” giant SEPs.
Background and Aims:: A growing body of literature has investigated the use of nonlinear analysis of electroencephalographic (EEG) signal and particularly the Hurst exponent as a method for studying EEG dynamics. In this paper we make an emphasis on investigation of the Hurst exponent in slow frequency bands in children during the first two years of life

Methods:: Retrospective cross-sectional study. The high-density EEG (128-channel) was recorded during wakefulness in one group typically developing infants in the following age points: 5 months (N=20 (F=7), mean age (ma)= 5.8 (0.2)), 10 months (N=18 (F=5), ma = 10.7 (0.3)), 14 months (N=18 (F=10), ma= 14.5 (0.5)).

The Hurst exponent ranges was calculated in MATLAB R2020a for delta (0.5-3.9 Hz) and theta (3.9-8 Hz) frequency band (0.1 Hz steps) in the next regions of interest (channels): frontal (3,4,5,6,10,11,12,13,16,18,19,20,23,24,27,28,29,111,112,117,118,123,124), central (7,10,30,31,35,36,37,41,55,80,87,104,105,106,110), temporal (34,40,46,47,51,58,59,91,96,97,98,102,109,116) and occipital (65,66,67,70,71,72,75,77,76,83,84,90).

Results:: The remarkable result of our study is identification of significant decrease of H values at 3.9-4.0 Hz for the estimated frequency bands in all regions of interest and in all age points.

Conclusions:: Results obtained from this study are similar to previously reported data (Hernan Diaz M. et al., 2015) indicating to sudden non-proportional decrease of H values of theta (> 4 Hz) frequency range, despite the discrepancy between chronological age of subjects and methodology of studies. However, this intriguing result is not clear from the point of view of its neurophysiological interpretation.
CORRELATION BETWEEN THE OCCURRENCE OF SEIZURES AND EEG RESULTS

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Background and Aims:: Epilepsy is a state of electrical signal disturbance in the brain that manifests as seizures. Diagnosis of epilepsy with history, physical examination, and investigations. One of the investigations that help diagnose epilepsy is electroencephalography (EEG). The EEG result is abnormal if there are epileptogenic and non-epileptogenic waves such as sharp waves, spike waves, and amplitude abnormalities. This study aims to determine the relationship between seizure frequency and EEG result.

Methods:: This type of research used in this research is observational analytic using the chi-square test. The data collection technique was carried out using the purposive sampling technique. The sample used in this study amounted to 300 samples that met the inclusion and exclusion criteria. This study's data were received through secondary data from the patient register by recording electroencephalography (EEG).

Results:: From 300 patients, the prevalence of patients with recurrent seizures would give a picture of abnormal EEG results compared to patients with one or two seizures. A firm agreement did obtain with the chi-square test between the seizure frequency and the EEG results (p = 0.050).

Conclusions:: There is a significant relationship between seizure frequency and EEG results.
Carpal Tunnel Syndrome: Prospective and Observational Study of 458 Cases. Diagnosis Accuracy of Clinical Symptoms and Their Correlation with ENMG Findings

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Background and Aims:: Electroneuromyography (ENMG) studies are the gold standard for carpal tunnel syndrome diagnosis (CTS). The main objective of this prospective study was to identify the clinical data and their concordance with ENMG test results in the first large series of CTS in Morocco.

Methods:: This study enrolled 249 patients diagnosed with CTS from February 2019 to December 2020.

Results:: This study concerned 458 cases of CTS, 93.2% females and 6.8% males with a mean age of 53 years. The average of symptoms duration until diagnosis was 33.43 months. CTS concerned especially housewives (48.19%). The associated comorbidities were found in 34.9%. The main complaint was pain and paresthesia in the territory of the median nerve in 79.98%, isolated ulnar nerve territory in 0.98% and isolated radial nerve territory in 1.22%. The Tinel's and Phalen's tests indicated moderate sensitivity (39.7% and 27.69% respectively) and high specificity (88.8% and 89.38% respectively). According to ENMG test results, 11% was normal including transcarpal comparisons, while 408 had median nerve entrapments in carpal tunnel (85% bilateral, 11.8% in the right and 2.7% in the left), 10.29% had very severe CTS with reduced CMAP amplitudes and abolished sensory potentials; 70.58% had moderate to severe CTS with abnormal motor nerve conduction and decreased sensory response; 18.13% had a CTS demonstrable only in sensory nerve conduction tests. There was a significant correlation between the duration of the disease and the severity of CTS.

Conclusions:: ENMG studies are valuable tools in diagnosis and severity assessment of CTS, it should be performed after clinical examination.
HEREDITARY NEUROPATHY WITH LIABILITY TO PRESSURE PALSY PRESENTING AS BILATERAL FOOT DROP

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Background and Aims:: Hereditary neuropathy with liability to pressure palsy (HNPP) is a rare, autosomal dominant disorder that typically present with episodic, multifocal neuropathy and recurrent transient pressure palsies. However HNPP can be underdiagnosed or misdiagnosed due to its heterogeneity in clinical and electrophysiological presentation. We herein present a case of HNPP presenting with bilateral foot drop.

Methods:: A 22-year-old man developed a sudden onset of painless muscle weakness in his both legs. On neurological examination, he was found to have bilateral foot drop. Normoactive deep tendon reflexes and acute onset history was interpreted as a transvers myelitis mistakenly. Magnetic resonance imaging of the brain and whole spine, extensive blood tests and investigation of cerebrospinal fluid were all normal. Then, electromyography was performed.

Results:: Nerve conduction study showed sensory and motor polyneuropathy associated with multiple entrapment neuropathies including conduction block of the bilateral peroneal nerves at fibular head. These electrophysiological findings were compatible with HNPP but also sural sparing was observed. Genetic testing was performed and PMP22 gene analysis showed the typical deletion, 1.5 Mb in the distal region of the locus 17p.11.2.

Conclusions:: In this study we describe a case of HNPP misdiagnosed as transvers myelitis initially. Interestingly, electrophysiological studies showed sural sparing that is classical finding of autoimmune polyradiculoneuropathies.
SEASONAL VARIATION OF GUILLAIN-BARRÉ SYNDROME IN IRANIAN PATIENTS: A RETROSPECTIVE STUDY

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Background and Aims:: It seems that the incidence of Guillain-Barré syndrome (GBS) has seasonal trends depending on weather as well as environmental and demographic factors such as upper respiratory tract (URI) and gastrointestinal (GI) infections as recent triggers, which might be higher in special weather conditions.

Methods:: The records of all admitted patients to all wards of Shariati Hospital with a probable diagnosis of GBS were investigated from March 2009 to March 2019 based on fulfillment of Brighton criteria and symptom onset during the recent 4 weeks.

Results:: Eighty-seven patients were included in this study of whom 63.2% were men. The mean age of the patients was 49.1±19.2 years, and 41.3% and 10.3% of the patients had recent URIs and GI infections, respectively. Most of the patients had acute inflammatory demyelinating polyneuropathy (AIDP) in electrophysiological study. The frequency of GBS in different seasons was 35.6% in the winter, 27.6% in the autumn, 19.6% in the spring, and 17.2% in the summer. The highest frequency was observed in January followed by September (16.1% and 14.9%, respectively). The lowest frequency was in July (3.4%). The most frequent electrophysiological subtype was AIDP in all seasons. The most common GBS disability score was 1. Mortality was 11.5% (6 men and 4 women). Six participants had acute motor sensory axonal neuropathy (AMSAN) and others had AIDP. No seasonal variation was detected.

Conclusions:: The highest and the lowest occurrence was seen in the winter and summer, respectively. AIDP was the most common electrophysiological subtype in all seasons.
MOVEMENT RELATED CORTICAL POTENTIALS AND MEANINGFUL DRAWING

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Background and Aims:: Movement related cortical potentials are usually studied employing single and well defined movements, thus lacking adherence to reality of complex gestures. Our research was aimed at investigating the possibility of triggering EEG recordings during natural freehand drawing and assessing if differences could be established between meaningful and meaningless movements.

Methods:: We used a digital drawing tablet to provide a trigger pulse every time a pen touched its surface. Five subjects were asked to execute a meaningful drawing or to simply draw meaningless curves. The EEG was recorded from C3-Au1 derivation and approximately 150 pen down events triggered the averaging of 600 ms before to 600 ms after trigger.

Results:: In meaningful drawing a slow negative deflection preceded the pen down event peaking at -140ms followed by a sharp and large positive to negative component with peaks few millisecond before and after the pen down. Slower components followed until about +400ms. The maximum peak to peak amplitude ranged between 6 and 4 microV across subjects. In meaningless drawing amplitude of the components occurring before pen down was reduced by approximately 70%, with little change in latency. No significant change in amplitude was detected after pen down.

Conclusions:: Our recordings demonstrate that it is possible to detect cortical events occurring before, during and after an event triggered by fast, natural and complex movements like freehand drawing. Cortical activity occurring before movement was remarkably increased by saliency.
SPECTRAL ANALYSIS OF HEART RATE VARIABILITY IN HUMAN FEAR LEARNING

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¹University of Bologna, Department Of Psychology, Bologna, Italy, ²University of Bologna, Department Of Electrical, Electronic And Information Engineering, Bologna, Italy, ³Politecnico di Milano, Department Of Electronics, Information And Bioengineering, Milano, Italy

Background and Aims:: Understanding transient dynamics of autonomic control during emotional learning is crucial to translate basic research into the treatment of psychopathology. Fear learning typically elicits short-latency bradycardia in humans. Yet, standard analyses of heart rate variability (HRV) fail to disentangle the contribution of parasympathetic and sympathetic activation, and to capture phasic changes of HRV during fear learning.

Methods:: To this aim, 50 healthy participants (mean age = 24 years) underwent a fear conditioning and extinction protocol. Two novel approaches were used to perform a frequency-domain analysis of HRV: short-time Fourier transform and instantaneous spectral estimation. Specifically, we tested whether the spectral components of the HRV, used as a non-invasive biomarker of sympathetic and parasympathetic activity, are able to distinguish between fear conditioned and neutral stimuli.

Results:: We found that learned fear elicited a profound heart rate deceleration in anticipation of noxious stimuli. More importantly, results revealed significant increases in spectral power in the high-frequency (0.15–0.40 Hz) band, indicating a specific vagal contribution, which robustly and reliably distinguished conditioned from neutral stimuli during fear learning.

Conclusions:: These results provide unique evidence of the direct involvement of the parasympathetic (vagal) component of the autonomic nervous system during fear learning. These laboratory findings can be readily translated into the clinical field, thereby providing a novel and accessible tool to evaluate several psychopathological processes, and quantify deficits of Vagus nerve modulation of HRV during emotional responding in humans.
Motor unit potential analysis in myasthenia gravis disease

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Background and Aims:: Motor unit action potential (MUAP) analysis is a test used to evaluate neuromuscular diseases (myopathy, neuropathy and neuromuscular junction disorders). Myasthenia gravis is an autoimmune disease affects neuromuscular junction that is diagnosed by clinical, pharmacological, serological and electrophysiological tests. This study was conducted to estimate parameters of MUAP analysis test in myasthenic patients based on our own control values.

Methods:: MUAP test was done in twenty healthy subjects and thirty-three myasthenic patients using concentric needle electrode. Four muscles were tested (extensor digitorum communis (EDC), tibialis anterior, frontalis and orbicularis oculi) muscles.

Results:: Comparison of MUAP analysis parameters (amplitude, duration, phases and turns) between control and myasthenic patients showed no significant differences regarding (EDC, Tibialis anterior and Frontalis) muscles, except Orbicularis oculi muscle which showed significant difference in amplitude and duration between control and myasthenic patients (p value <0.02).

Conclusions:: MUAP parameters of myasthenic patients exhibited normal values in most of the tested muscles.

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Background and Aims:: Body Mass Index (BMI) is a measuring instrument in determining of a person's nutritional status. Obesity and Overweight are the risk factors for Carpal Tunnel Syndrome (CTS). This study was conducted to determine the relationship between BMI and the severity level of CTS at RSUP Dr. M. Djamil Padang Period 2017-2018

Methods:: This type of research is analytic with cross-sectional design. The sample of this study was CTS patients in the Neurology Department of Dr. RSUP M. Djamil Padang and Electromyography (EMG) examination with a sample size of 34. Sampling was done by total sampling technique based on inclusion and exclusion criteria. The instruments of this study were medical records and EMG results of CTS patients at RSUP Dr. M. Djamil Padang. Data was analyzed using the fisher’s exact test.

Results:: The majority of CTS patients were female (85.3%). The majority age group is 46-55 years (32.4%). Bilateral CTS is the most common symptom of CTS (85.3%). The BMI of CTS patients was found to be obese (38.2%) and normal (38.2%). Severe CTS (38.2%) is the most degree of severity found. Bivariate analysis showed the value of p = 0.03 (p <0.05), where there was a significant relationship BMI and the severity of CTS.
<table>
<thead>
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<th>Variable</th>
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<td></td>
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<tr>
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<td>5</td>
<td>14.7</td>
</tr>
<tr>
<td>Woman</td>
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<tr>
<td>Bilateral</td>
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<td>76.5</td>
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</table>
Conclusions: In this study there was a relationship between body mass index and the severity of CTS. Therefore, it is expected to provide health promotion and education related to obesity or overweight and its relationship with CTS given the high level of morbidity from this situation.

<table>
<thead>
<tr>
<th>Body Mass Index</th>
<th>Severity of CTS</th>
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<tr>
<td></td>
<td>Mild</td>
<td>f</td>
<td>%</td>
<td>Severe</td>
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<tr>
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<td>16</td>
<td>47,1</td>
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<tr>
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<td>11</td>
<td>32,3</td>
<td>23</td>
<td>67,7</td>
<td>34</td>
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</tbody>
</table>

p value 0,03
TRANSCALLOSAL MOTOR DISINHIBITION TO TRANSCRANIAL MAGNETIC STIMULATION IN DE NOVO PATIENTS WITH CELIAC DISEASE

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Background and Aims:: Celiac disease (CD) may present or be complicated by neurological and neuropsychiatric manifestations. Transcranial magnetic stimulation (TMS) non-invasively probes brain excitability, even in preclinical stages. We previously demonstrated an intracortical motor disinhibition and hyperfacilitation in de novo CD patients, which revert back after long-term gluten-free diet (GFD). In the present study we explored the intercortical excitability by transcallosal inhibition, which has never been investigated in CD.

Methods:: 15 right-handed de novo CD patients and 15 age-matched healthy controls were screened for cognitive and depressive symptoms to the Montreal Cognitive Assessment (MoCA) and the 17-item Hamilton Depression Rating Scale (HDRS), respectively. TMS consisted of resting motor threshold, latency and amplitude of the motor evoked potentials, latency and duration of the contralateral silent period (cSP). Transcallosal inhibition was evaluated as onset latency and duration of the ipsilateral silent period (iSP).

Results:: Patients had worse MoCA and HDRS scores. cSP and iSP durations were also shorter in patients, with a positive correlation between MoCA score and iSP duration.

Conclusions:: An intra- and intercortical disinhibition was observed in neurologically asymptomatic CD patients, suggesting the involvement of GABA-mediated intracortical and callosal circuitries. Early diagnosis and prompt GFD are needed to prevent cognitive and mood changes in CD.
INTER-ELECTRODE DISTANCE INFLUENCES SUBTHALAMIC LOCAL FIELD POTENTIALS RECORDINGS IN PARKINSON’S DISEASE

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Background and Aims:: The study of subthalamic (STN) local field potentials (LFPs) led to significant advancement in the understanding of the pathophysiology of Parkinson’s disease (PD). PD is associated with pathological spectral power in the β band (11–30 Hz range), and it is also characterized by β phase-high frequency (200-500Hz) amplitude coupling (PAC). Although both β band spectral power and PAC correlate with PD severity, whether their changes are consistent with different electrodes geometry is still a matter of debate. This study aims to assess the spectral power and PAC of two LFP signals captured from both wide- and close-spaced contact pairs (i.e. 0-3 and 1-2) of the same DBS electrode within the STN, before and after Levodopa administration.

Methods:: LFP12 and LFP03 were recorded from 20 PD patients. We evaluated oscillatory power, PAC and correlation with motor symptoms (UPDRSIII) between close- and wide spaced electrodes.

Results:: Before Levodopa, both LFP03 and LFP12 power in the α band correlated with UPDRSIII. Whereas the low-β (12-20Hz) band did not differ between the two contacts, lower frequency bands had higher power in LFP03 than in LFP12. After Levodopa, a modulation of the low-β power and an increased β-LFO (15-45Hz) PAC was found only for LFP12.

Conclusions:: These results may be relevant for the implementation of better control strategies for adaptive Deep Brain Stimulation (aDBS). LFP12 can be used to detect β power (i.e. bradykinesia), while LFP03 are optimal for low frequency oscillations (dyskinesias).
EFFECTS OF NEURAL STEM CELL-DERIVED EXOSOMES ON HFD-DEPENDENT IMPAIRMENT OF BRAIN PLASTICITY: MOLECULAR AND FUNCTIONAL EVIDENCE

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Background and Aims:: Adult neural stem cells (NSC) release extracellular vesicles (exo-NSC) contributing to intercellular communication and potentially capable to influence brain cell activity and modulate brain plasticity. High fat diet (HFD) in C57BL/6 mice is a well-established experimental model of obesity and insulin resistance, almost completely resembling the hallmarks of metabolic syndrome and cognitive decline identified in humans. We investigated whether administration of exo-NSC prevented alterations of hippocampal synaptic plasticity and adult neurogenesis induced by insulin resistance.

Methods:: C57BL/6 mice were fed with standard diet or HFD and intranasally treated with vehicle or exo-NSC for 6 weeks. NSCs were cultivated in vitro with a medium containing insulin and palmitic acid (IPA) for 3 days to mimic insulin resistance. Biochemical and imaging techniques have been used to analyze IPA, HFD and exo-NSC effects on NSCs in vitro and in vivo.

Results:: Our data demonstrated that intranasal administration of exo-NSC was able to deliver the vesicles into the hippocampus of mice and to restore the HFD-dependent proliferation/senescence unbalance of neurogenic niche. Chronic exo-NSC administration also prevented HFD-induced memory impairment. Interestingly, exo-NSCs appear to differently modulate intracellular signaling cascades in mature neurons and NSCs. In particular, exosomal cargo containing neurotrophic factors (e.g., BDNF) reactivated CREB-dependent expression of synaptic plasticity-related genes in differentiated neurons. In addition, exo-NSC restored insulin signaling and epigenetically regulated FoxO-dependent transcriptional activity in NSCs.

Conclusions:: Our findings highlight the role of extracellular vesicle cargo in the regulation of brain plasticity and provide evidence of the potential therapeutic effect of exo-NSC against metabolic disease-related cognitive deficits.
HIPPOCAMPAL ERK1/2 ACTIVATION CONTRIBUTE TO SEX DIFFERENCES IN RETROACTIVE INTERFERENCE.

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\textbf{Background and Aims::} Memory removal is a physiological function and little is known about its molecular and cellular underpinnings. One mechanism for removing stored information from the brain is retroactive interference, a phenomenon in which newly acquired information overwrites or interferes with the retrieval of previously stored memories. In this work, we investigated the behavioural and molecular differences in a retroactive interference paradigm between male and female mice.

\textbf{Methods::} For the novel object recognition interference paradigm (NOR-Int), C57Bl/6 mice underwent a 5 minutes training session with a couple of objects. One hour prior to the test with one new object and one training object, animals were exposed to a different couple of objects unrelated to the training or test objects (interference session). For immunohistochemical and molecular experiments, animals were sacrificed at different time points post-interference and c-fos expression and ERK1/2 activatory phosphorylation were assessed.

\textbf{Results::} In the NOR-Int paradigm, female mice were able to discriminate the novel object while male mice showed impaired memory performance. Immunohistochemical analysis of c-fos expression showed a stronger activation of female dorsal dentate gyrus post-interference compared to males. Western blot analysis revealed a higher level of ERK1/2 activatory phosphorylation in the hippocampus of female mice compared to male mice post-interference. Finally, injection of an ERK1/2 inhibitor into the dorsal hippocampus of female mice prior to the interference procedure rendered females susceptible to the interference-mediated memory removal.

\textbf{Conclusions::} Collectively, our data suggest that hippocampal ERK1/2 activation contribute to a pattern separation mechanism which reduces object-related retroactive interference in female mice.
CLINICOEPIDEMIOLOGICAL AND ELECTROPHYSIOLOGICAL STUDY OF PERIPHERAL NEUROPATHY IN HIV-INFECTED PATIENTS

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Background and Aims:: Peripheral neuropathy (PN) is one of the most prevalent neurologic complications of HIV infection and frequently inadequately treated in resource-limited settings. Despite substantial improvements in the general health of HIV-infected patients throughout HAART, PN continues to be a crucial aspect of patients' morbidity due to its severe impact on their quality of life. More than two-thirds of HIV patients may have an abnormality in electrophysiology study before their symptoms occurred. Hence, understanding the abnormality in electrophysiology study in HIV patients and the association with risk factors and degree of PN is imperative. Aim: To identify risk factors for PN in HIV patients and examine electrophysiological abnormalities concerning disease severity.

Methods:: The study used a cross-sectional design and lasted around one year. The study enrolled patients seen in the outpatient department of an antiretroviral therapy (ART) center. Selected individuals were evaluated for peripheral neuropathy-related signs and symptoms and underwent electrophysiological examination.

Results:: There was a strong association between CD4 nadir, smoking, and comorbidity with toxoplasma, CMV, tuberculosis, and hepatitis infection in PN. The most prevalent pathogenic feature of neuropathy was mixed neuropathy (both axonal and demyelination). In addition, there was a significant correlation between the severity of peripheral neuropathy and the results of electrophysiological studies in the sensory and motoric median nerves, as well as the motoric ulnar, tibial, and peroneal nerves.

Conclusions:: Addressing risk factor may help to minimize the incidence of PN. In addition, early detection and prompt treatment of HIV may help slow the progression of nerve damage in HIV patients.
PHYSIOTHERAPY WITH DUAL-TASKS IMPROVES COGNITION IN PARKINSON’S DISEASE WITH POSTURAL INSTABILITY AND GAIT DISORDERS

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Background and Aims:: To assess cognitive changes following a 6-week training associated with dual-task gait/balance exercises in PD patients with postural instability and gait disorders (PD-PIGD).

Methods:: 25 PD-PIGD patients were randomized into 2 groups: i) action observation training (AOT) and motor imagery (MI)+DUAL-TASK group performed a 6-week (W6) training consisting of AOT-MI combined with practicing observed-imagined gait and balance exercises; ii) DUAL-TASK-group performed the same exercises combined with landscape-videos observation. At baseline, W6 and W14, patients underwent neurological, computerized cognitive and motor evaluations. 23 healthy controls underwent a neuropsychological assessment at the study entry only. Cognitive changes in patients were monitored with the CANTAB (Cambridge Neuropsychological Test Automated Battery). Cognitive changes at each time point in the overall PD-PIGD sample and between groups (AOT-MI + DUAL-TASK and DUAL-TASK) were assessed.

Results:: At baseline, no cognitive differences were found between the two PD-PIGD groups. However, both PD groups performed worse than healthy controls in several cognitive domains. Over time, both PD groups improved in terms of gait velocity and balance. Regarding cognitive changes, at W6 and W14, all PD patients improved in terms of accuracy and reaction times in tests assessing attention switching and visuospatial localization abilities. No differences were observed between groups over time.

Conclusions:: A physiotherapy approach associated with dual-task gait/balance exercises can improve cognitive performances in PD-PIGD patients that persist at long term. This improvement is evident in specific cognitive domains, which are usually affected in PD-PIGD and can interfere with their motor performances.
A RANDOMIZED CONTROLLED TRIAL COMBINING COMPUTERIZED COGNITIVE TRAINING AND TRANSCRANIAL DIRECT CURRENT STIMULATION IN THE EARLY STAGES OF COGNITIVE IMPAIRMENT

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Background and Aims:: The prevalence of neurodegenerative diseases is expected to increase over the next years, therefore new methods able to prevent and delay cognitive decline are needed. The aim of this prospective double-blind 2-arm Randomized Controlled Trial was to evaluate the effectiveness of a combined treatment protocol associating an computerized cognitive training with anodal transcranial direct current stimulation (tDCS).

Methods:: Thirty-three patients (14 females; mean age = 74.18, SD = 5.59) in the early stage of cognitive impairment (i.e. with a diagnosis of aMCI or mild AD) were enrolled and randomly assigned to the experimental group (CoRe + real tDCS) or control group (CoRe + sham tDCS). All patients were evaluated with an exhaustive neuropsychological assessment before (T0) and after (T1) treatment. A post-treatment follow-up visit was scheduled 6 months (T2) after the end of the treatment. Treatment consisted in 12 individual sessions of about 45 minutes of cognitive training with multi-domain CoRe combined with online tDCS. Being adaptive, CoRe allows the possibility to generate different patient-tailored exercises.

Results:: We found that patients who received the real stimulation improved in working memory and attention/processing speed at both T1 and T2. Moreover, they reported a stable global cognitive functioning (MMSE) at T2, while patients in the control group worsened. In addition, age, mood, and initial cognitive functioning resulted to play a role in predicting treatment effects.

Conclusions:: Our findings confirm the importance of adopting a combined (i.e. cognitive training + tDCS) multi-domain intervention, as it may facilitate the development of compensatory mechanisms.
COMPARISON OF THE EFFECTIVENESS OF MOTOR AND COGNITIVE REHABILITATION ALONE COMPARED TO THE COMBINATION OF THE TWO IN PATIENTS WITH MULTIPLE SCLEROSIS

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Background and Aims:: Motor and cognitive impairments (CI) are the main clinical features of Multiple Sclerosis (MS) with an incidence of around 85% for the former and 65 % for the latter. Aim of the present study was to compare three formats of cognitive and motor rehabilitation programs in order to understand which is the most efficient in reducing cognitive deficits in MS patients.

Methods:: A total of 48 patients were randomly assigned to one of the three rehabilitation conditions (two cognitive training/week-C1; one cognitive and one motor training/week-C2; two motor training/week-C3, for 12 weeks). All participants were submitted to a detailed neuropsychological and motor assessments before (T0) and after (T1) the treatment. The cognitive rehabilitation was focused on memory functioning and performed with Rehacom (http://www.emsmedical.net).

Results:: No significant differences in age, sex, education and disease course was found between the three conditions. In the C1 condition we found a decrease in the total cognitive impairment score. In C3 no statistical difference was found between T0 and T1 for any cognitive or motor variable. Conversely, patients in the C2 group showed an improvement in both gait and the 2 memory tasks.

Conclusions:: These preliminary data confirm that MS patients may benefit more from a combined approach (cognitive and motor) than from separate single training conditions (C1 and C2). Rehabilitation programs combining motor and cognitive treatments could give a stronger advantage in the improvement of cognitive impairment due to MS.
EFFECT OF EXTRACORPOREAL SHOCK WAVE THERAPY AND BOTULINUM TOXIN INJECTION ON NERVE REGENERATION IN EXPERIMENTALLY INDUCED SCIATIC NERVE INJURY RATS

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Background and Aims:: Extracorporeal shock wave therapy and Botulinum neurotoxin A have recently been studied as modalities for neural regeneration. The goal of this study is to investigate whether neural regeneration and functional recovery improved by using BoNT/A and ESWT as a non-surgical treatment.

Methods:: After crushing the sciatic nerve of 60 rats, intranerve delivery of BoNT/A or transcutaneous ESWT was applied. Two experimental groups and one control group were set up: the group 1(G1) received intranerve delivery of BoNT/A(15pg) and group 2(G2) received ESWT(400 impulses,4 Hz, 1 session). Both groups were treated immediately after nerve injury. A group 3(control, G3) received nerve injury only. Molecular biology and histological exams of the sacrificed rats were confirmed after 3, 6, and 10 weeks of experiment. The antibodies used were GFAP, GAP43, NF200, ATF3, S100 assessed by realtime PCR, Western blot, ELISA and Immunofluorescence. Neural regeneration of all rats was measured weekly by Sciatic Function Index(SFI) and nerve conduction study(NCS).

Results:: It was confirmed that G1 and G2 were more highly expressed in all five genes than in G3. In the NCS, G1 and G2 showed statistically significant differences compared to G3, and G1 showed the highest value. According to the SFI results, G1 and G2 improved gait pattern compared to G3 statistically significant at weeks 1, 2, 3 and 4.

Conclusions:: Collectively, these findings indicate that both ESWT and BoNT/A are helpful in neural regeneration and function improvement after peripheral nerve injury. And they are expected to be promising as the effective treatment modalities for neural regeneration.
"DEVELOPMENT OF VIDEOGAMES TO IMPROVE THE FUNCTIONALITY OF THE UPPER LIMB IN NEUROLOGICAL PATIENTS".

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Background and Aims:: Today, one of the challenges facing neurorehabilitation is that people who have suffered a neurological event can be completely independent in their daily life activities. One of the most frequent sequelae in these patients is the limitation of the movement of upper limb. The new technologies can improve functional independence. Objective: Develop a videogame to improve the functionality of the upper limb in the activity of feeding for adult and childhood neurological patients.

Methods:: A videogame was built that incorporates the movements required to put your hand to your mouth. The video game incorporates 9 mini-video games, which train different planes of movement with three levels of difficulty. To determine the reference values for the design of the video game, the reference values of normal range of motion and measurements of joint ranges obtained during the activity in neurological patients were used. A Kinect camera and the Unity web platform were used to capture movements. Finally, pilot tests were carried out with children and adults for the final version.

Results:: The videogame "My space travel" was developed, which allows the training of the affected upper limb in different planes of movement, considering the movement characteristics of people with neurological damage.

Conclusions:: The development of technologies in rehabilitation should consider not only the specific objectives that are to be achieved in this, but the population for which they are being designed, therefore, it is important that more and more rehabilitation professionals be involved in the design and elaboration of these.
Background and Aims:: Stroke is the leading cause of death, disability and hospitalization (> 65 years) in Chile. A large part of post-stroke patients remain with alterations of the upper limb, among them the involvement of property perception and sensitivity, which is why the need for the implementation of a specific program. Neurocognitive physiotherapy is a treatment little used in Chilean rehabilitation, which focuses on a sensory-motor reeducation to restore sensitivity and functionality. Objective: To determine the effectiveness of a neurocognitive physiotherapy intervention program in the sensitivity and functionality of the upper limb in patients with ACV in the subacute and chronic stage, belonging to the city of Valdivia.

Methods:: Quasi-experimental study with a study group, allocation for convenience, without masking. Eight participants were analyzed with LCA (med = 57.00, RIC [27-82].) The program was applied during 6 sessions of 45 minutes.

Results:: The neurocognitive intervention was able to obtain a significant difference in motor function (p = 0.01), sensitivity (p = 0.00), joint movement (p = 0.00). The rest of the variables did not show significant differences.

Conclusions:: Neurocognitive physiotherapy produces significant changes in upper limb function in acute and chronic stroke patients.
EFFICACY OF HIGH-INTENSITY LASER THERAPY ON MECHANICALLY INDUCED SCIATIC NERVE INJURY IN WISTER RATS.

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Background and Aims:: Background: Traumatic nerve injury (TNI) is a common source of motor disability. Early application of low-level laser therapy promotes the regeneration of nerves in TNI with a lack of evidence of high-intensity laser therapy (HILT) on nerve regeneration. Aim: The purpose of the study was to evaluate the efficacy of HILT in the treatment of mechanically induced sciatic nerve injury in Wister rats.

Methods:: A total of 60 male Wistar rats were randomized into three groups. Groups received no crushing-no laser, crushing without laser, and crushing plus HILT for control negative, control positive, HILT group respectively. At the thigh area, the left sciatic nerve was exposed, crushed, and received HILT (λ=1064 nm, 10.5 W, 20 Hz, 50 J/cm², 12 min.) five times/ week for three weeks. Gait and electrophysiological evaluations were measured weekly for three weeks by sciatic functional index (SFI), the amplitude of compound motor action potential (CMAP), and motor nerve conduction velocity (MNCV). The level of significance was set at p<0.05.

Results:: There were no significant effects of the measured variables after one week. After two weeks, there were significant increases in the amplitude of the CMAP and MNCV in the HILT group with non-significant changes in the control groups. A significant decrease in the SFI was observed after three weeks of HILT as compared to controls.

Conclusions:: HILT promotes the recovery of the sciatic nerve by increasing the amplitude of CMAP and MNCV and decreasing the SFI in mechanically induced sciatic nerve injury in Wister rats.
EFFECTS OF ISOMETRIC SCAPULAR EXERCISES ON THE SCAPULAR STABILITY IN PATIENTS WITH STROKE

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Background and Aims:: Maintaining the scapular alignment and stability has a key role on upper extremity functionality in neurological disabilities. The aim of this study was to examine the effect of scapular exercises on the scapular stability in patients with stroke.  
Methods:: Patients (aged 50-85 years) with acute hemiparetic stroke were divided into two groups as control group and study group by simple randomization method. A physical therapist, who was blinded to which group they belonged, evaluated the participants before and after treatment. The exercises were applied by another physiotherapist. The patients in both group were treated with the exercise program according to the Bobath concept and isometric scapular exercises were applied to the study group in addition to these exercises. The evaluation instruments included measurement of scapular position.  
Results:: After 5 sessions, a significant improvement was found distance in protraction and distance between protraction and retraction at 90° of shoulder flexion, distance in protraction, retraction and distance between protraction and retraction at 90° of shoulder abduction within both groups and distance in protraction at 90° of shoulder flexion within only control group.  
Conclusions:: The increase in the ability of the scapula to contract isometric can also increase the quality of scapular movements by increasing the dynamic stability of the scapula.
EFFECT OF WHOLE-BODY VIBRATION ON FUNCTIONAL CAPACITY AND RESPIRATORY FUNCTIONS IN INDIVIDUALS WITH STROKE: A RANDOMIZED CONTROLLED STUDY

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Background and Aims:: Decreased functional and pulmonary capacity are among the most frequently overlooked non-motor symptoms experienced in patients with stroke. The aim of this study was to determine the effects of 4-week whole body vibration (WBV) approach in addition to neurodevelopmental treatment (NDT) on functional capacity and respiratory functions in patients with stroke.

Methods:: Twenty-eight patients with stroke were divided into 2 groups as treated by NDT (control group) and NDT+WBV (intervention group). Patients’ pre and post-treatment results were evaluated with six-minute walking test (6MWT) for functional capacity, a microQuark® brand spirometer for respiratory volume and capacity, and chest circumference measurements for thoracic expansion ability.

Results:: The increase in walking distance and VO₂max levels in the NDT+WBV group were significantly higher than the NDT group (p<0.05). Both exercise approaches had a similar effect on both effort-related and non-effort-related developments in respiratory function’s flow and volume parameters, and chest circumference measurement results, except inspiratory capacity (p>0.05).

Conclusions:: Our results showed that the WBV applied in addition to NDT lead to gain more effective results for the treatment of the reduction in functional capacity and respiratory dysfunction observed in patients with stroke.
THE EFFECT OF WHOLE BODY VIBRATION ON SPASTICITY, DYNAMIC BALANCE AND SHOULDER PAIN IN PATIENTS WITH TAKAYASU ARTERITIS

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Background and Aims: Takayasu arteritis is a chronic inflammatory arteritis which affects mainly the aorta and its major branches. Vascular, neurological, musculoskeletal, constitutional and cardiac problems can be seen related with Takayasu arteritis. The aim of this study was to evaluate the effectiveness of combined physical therapy (PT) and whole body vibration (WBV) on spasticity, dynamic balance and shoulder pain.

Methods: This case was a 55-year-old male who presented with balance impairment, shoulder pain, upper an lower extremity dysfunction. The patient completed 8 weeks of PT and WBV. After the recording demographic characteristic, baseline clinical measurements including Modified Ashworth Scale, Time up and go test and visual analog scale to assess the spasticity, dynamic balance and shoulder pain were applied to case, respectively. The assessments were repeated twice after the first and last session of treatment. Follow-up measurements will be performed in the third and sixth months after treatment.

Results: About 10% improvement on dynamic balance and more decreased spasticity degree of upper and lower extremity muscles was seen after the first episode of therapy than 8 weeks of treatment. After completing all sessions, the following changes were noted from baseline: 21% improvement on dynamic balance, 26% improvement on shoulder pain. Finger and wrist flexor and gastrocnemius muscles spasticity decreased from 3 to 2.

Conclusions: This case report suggests that combined of PT and TVV of Takayasu arteritis was effective in helping to improve dynamic balance and to decrease the spasticity, and shoulder pain.
SAFETY AND EFFICACY OF MLC601/MLC901 (NEUROAID) AMONGST PATIENTS WHO SUSTAIN SEVERE SPINAL CORD INJURY (SATURN STUDY)

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Background and Aims:: Objective This pilot study aims to evaluate the safety and efficacy of MLC601/MLC901 among subjects with moderately-severe to severe SCI. Background Spinal cord injury has been considered an incurable condition and it often causes devastating sequelae. Hence the growing emphasis on the need for multimodal therapeutic approaches. MLC601/MLC901 (NeuroAid) are natural formulations demonstrated to enhance neurological recovery after injury and extensively studied in stroke and traumatic brain injury.

Methods:: Methods This prospective, phase I trial (ClinicalTrials.gov Identifier: NCT02537899) includes subjects with moderately-severe to severe SCI: American Spinal Injury Association (ASIA) Impairment Scale (AIS) grades A and B. Subjects received open-label MLC601/MLC901 for 6 months in addition to standard care and followed up for 24 months. Rates of adverse events, progression of neurological status (AIS) and functional outcome (SCIM), Short Form (SF-8) Health Survey were evaluated at month 1, 3, 6, 12, 18 and 24.

Results:: Results This analysis included 30 patients with the mean age of 42.2 years old, the median time from injury at 15.5 days, and median time to first dose at 16.5 days. The most common reasons for injury were Motor Vehicle Accident (MVA) (43.3%). SATURN met its primary endpoint of showing improvement in total motor score at 6 months compared to baseline (19.4 SD± 24.5, 95% CI, 9.1 to 29.7; P < 0.001). There were 4 patients (13.3%) who reported at least one adverse event.

Conclusions:: Conclusions MLC601/MLC901 shows remarkable promise as a safe adjunctive for aiding recovery in our cohort of subjects with moderately-severe to severe SCI.
MONITORING OF MOTOR DEFICITS DYNAMICS IN PATIENTS AFTER LUMBAR HERNIATED DISK REMOVAL.

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Background and Aims:: According to the current literature, the neurological deficit after the removal of a disc herniation at the lumbar level in the postoperative period ranges from 22% to 39%. The aim. Objective evaluation of motor deficits in the distal lower extremities in patients operated on lumbar herniated disk using isokinetic dynamometry.

Methods:: Prospective study. In the period from 2018 to 2020, the results of surgical treatment of 66 patients with lumbar spine hernias with compression radiculopathy were analyzed. Men 34, women 32, average age 41.0+3.2 years. The strength and volume of the lower leg muscles were measured using the isokinetic dynamometer. The isokinetics, isometry in the concentric and the eccentric were evaluated, both in the affected limb and in the healthy one. The dynamics of the pic torque (PT) and the retention time of PT (TPT) were evaluated. The patients were examined before the operation, 14, 90 days after the operation.

Results:: Compression radiculopathy L5 was detected in 25 patients, S1– in 41. When assessing the muscle strength in the eccentric before surgery, the decrease in the concentric of the affected limb relative to the healthy one with the lesion of the L5 root was 41.7%, with the lesion of the S1 root-47.5%. Immediately after the operation, the strength in the lesion of m.tibialis anterior was restored- 84.9%, in the lesion of m. gastrocnemius to 81.7%.

Conclusions:: The use of isokinetic dynamometry is advisable in the objective assessment of muscle strength after the removal of root compression during the removal of a lumbar disc herniation.
THE EFFECTS OF NEUROREHABILITATION ON SEQUENCE EFFECT IN PARKINSON'S DISEASE PATIENTS WITH AND WITHOUT FREEZING OF GAIT

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Background and Aims:: Freezing of gait (FOG) represents a disabling symptom of Parkinson’s disease (PD). The sequence effect (SE), an amplitude reduction of repetitive movements, is a clinical feature of several tasks in PD. We studied the effects of an overground training rehabilitative program on SE in PD patients with and without FOG.

Methods:: Forty-three PD patients (30 males, 70.6±7.5 years old) were enrolled. The patients completed a 4-week in-hospital rehabilitation program, (6 sessions per week - 90 minutes each). At hospital admission (T0) and at the end of the rehabilitation (T1), the patients underwent instrumental gait analysis. SE was computed as a regression slope (β) of step length. The lengths of the last six steps ahead of the final stride were plotted against step number, and the linear regression slope (β) was calculated as a measure of SE.

Results:: Twenty-three patients were affected by FOG (PD-FOG: 19 males, 72.4±5.6 years) while the remaining 20 did not (PD-NO FOG: 11 males, 68.4±8.9 years). The SE was more negative in PD-FOG group (-0.80±0.6) when compared to PD-NO FOG group (-0.39±0.3) (p=0.007). The SE improved at the end of the rehabilitation period in the study population (T0: -0.63±0.5; T1: -0.23±0.4; factor TIME: p=0.001). A significant TIMExGROUP interaction (p=0.012) was consistent with a more pronounced improvement of SE in PD-FOG group when compared to PD-NO FOG group.

Conclusions:: SE is pronounced in PD patients affected by FOG. A 4-week rehabilitation positively modulated the SE in PD patients, specifically in the PD-FOG group.
Background and Aims:: There is a close connection between the central nervous system and the immune system. This balance can be impaired in the presence of severe brain damage, i.e. in case of stroke. The consequences of stroke on the balance between these two systems are cerebral inflammation and immunosuppression. The aim of this study is to verify whether lymphopenia may represent a negative prognostic index of functional recovery in the Neurorehabilitative setting.

Methods:: Fifty-six stroke patients (42 ischemic and 14 haemorrhagic), were enrolled. The patients completed a 8-week in-hospital rehabilitation program, (6 sessions per week; 90 minutes each). At hospital admission (T0) and at the end of the rehabilitation (T1), the patients underwent: neurological and functional physical evaluation examination, administration of clinical scales, and inertial gait analysis. In this study, 1500 lymphocytes/µl were used as cut-off for lymphopenia definition.

Results:: At T0, 17 patients (30.4%) had lymphopenia. At T0, they were older and more disabled than patients without lymphopenia. The percentage of infectious complications was significantly higher in the group with lymphopenia (58.8%) than in the group without lymphopenia (28.2%) (p=0.039). The presence/absence of lymphopenia was not a predictor of the effectiveness of the rehabilitation treatment, although outcome scores of patients without lymphopenia were still slightly better at hospital discharge (T1).

Conclusions:: In stroke patients, lymphopenia may represent a complication of the rehabilitative setting. Patients with lymphopenia were more disabled at hospital admission and discharge, even if the extent of improvement was comparable to non-lymphopenic patients. Lymphopenia was a strong predictor of infectious complications.
SUBACUTE PROGRESSIVE PARAPARESIS (FOIX-ALAJOUANINE SYNDROME) IN AN ELDERLY AFRICAN-AMERICAN MAN

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Background and Aims:: First described in 1926 by Foix and Alajouanine, the Foix-Alajouanine syndrome is a rare congestive myelopathy typically arising secondary to dural arteriovenous (AV) fistulas, often of cryptogenic origin. We here present a case of the rare and overlooked Foix-Alajouanine syndrome.

Methods:: A 68-year-old African American male with past medical history of coronary artery disease, hypertension, hyperlipidemia, and diabetes presented with chief complaint of three months of urinary and fecal incontinence accompanied by slowly progressive left followed by right lower extremity weakness. The patient also reported new-onset low back pain with symptoms worse towards the end of the day.

Results:: Initial exam demonstrated diminished muscle bulk and weakness against resistance in both legs, left worse than right and distal worse than proximal. The sensory examination showed symmetric hyporeflexia in the legs. The Babinski sign was negative. Serum and CSF labs were normal, including various tests for other causes of myelopathy. MRI was notable for cord edema from T6 to the conus medullaris. A spinal angiogram revealed an epidural AV fistula at the left L3 radicular artery with marked venous congestion in neighboring levels. Because the lesion was not amenable to endovascular repair the patient underwent successful open repair one month later, followed by an extended rehabilitation course to regain ambulatory ability.

Conclusions:: This case demonstrates many typical features of Foix-Alajouanine syndrome. Generally subacute to chronic, there is a predilection towards males over 50. Open surgery is often necessary. Advanced myelopathy portends worse outcomes. Early detection and surgical repair are critical.
NEW OPPORTUNITIES FOR REHABILITATION OF COGNITIVE AND SPEECH DISORDERS IN PATIENTS WITH ISCHEMIC STROKE

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Asfendiyarov Kazakh National Medical University, Department Of Nervous Diseases With A Course Of Neurosurgery, Almaty, Kazakhstan

Background and Aims:: The provision of specialized psychological and speech therapy assistance contributes to a more effective rehabilitation of patients with Ischemic stroke (IS) Objective: to evaluate the effectiveness of articulatory logotherapy and ion-reflex phonophoresis with hypothalamic phospholipids in the rehabilitation of patients with IS in the early recovery period.

Methods:: 154 patients with cognitive and speech disorders on the background of IS at the age of 42-68 years were studied. Of these, 36 with motor aphasia, 15 sensory aphasia, 18 amnestic aphasia, 85 with dysarthria. The MMSE short scale, MoCA test, Barthel ADL index, Rivermead questionnaire were used. For the first time, we tested the Speech Impairment Scale (SPR) as a measure of effectiveness. 84 patients underwent a course of ion-reflex phonophoresis with hypothalamic phospholipids, longitudinal psychological fronto-occipital galvanization of the head, intrapersonal correction, a restorative integrative “I” image, articulatory gymnastics and articulatory massage. Control - 70 patients.

Results:: There was a positive dynamics of speech functions according to SRR data (48.8 ± 1.6 - 78.86 ± 1.5); control (48.6 ± 1.6 - 57.88 ± 1.6) dynamics of cognitive functions in the main group (20.13 ± 2.3 - 26.0 ± 2.3) - control (20.2 ± 2, 1 - 23.2 ± 2.1). The Barthel Index climbed 19 points and the Rivermead Index climbed 18 points.

Conclusions:: The articulation logotherapy and ion-reflex phonophoresis with hypothalamic phospholipids allows to can achieve effective rehabilitation in patients with IS in the early recovery period. The use of SPR showed the effectiveness of therapeutic methods in speech disorders.
IS THE INTELLIGENCEGYM AN EFFECTIVE TOOL TO IMPROVE COGNITIVE PERFORMANCE IN VASCULAR DEMENTIA?

Nina Trushkova¹, Olga Cochran¹, Natalia Ermolina², Giovanni Zelano³
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Background and Aims:: Several studies have shown that the capacity of working memory (WM) could be an indicator of performance in several other cognitive tasks: from simple attentional tasks to tasks requiring more compound capabilities. There are many cognitive training strategies, but none of them uses more different cognitive activities during the class. We hypothesized that by changing activities during the class we will have more efficacy to improve cognitive abilities including WM. This study investigated the effectiveness of WM training created by us (IntelligenceGym) to improve cognitive functions in older adults with mild vascular dementia (VaD).

Methods:: The study subjects were 108 VaD patients, 42 men and 66 women, with Mini-Mental State Examination (MMSE) scores of 19 to 23 at inclusion. All of them had initially reduced WM capacity level. We have created two groups: Dual-Task Group and IntelligenceGym Group, each 27 people. We proposed them to perform training one hour twice a week for 24 weeks. Cognitive performance was assessed before and after intervention included MMSE, Forward and Backward Digit Span Test, Rey’s Auditory Verbal Learning test (RAVLT), TMT-A, TMT-B.

Results:: The cognitive assessment showed statistically significant improvement in all two groups in all the scores tested (t-test performed). The results showed that participants of the IntelligenceGym Group had significantly higher performance in Backward Digit Span Test, RAVLT and TMT-B, than the Dual Task Group.

Conclusions:: Our findings indicate that the IntelligenceGym training is an efficient tool to improve cognitive performance in older adults with VaD.
INNOVATIVE MOTOR LEARNING TRAINING IMPROVES PARETIC ARM FUNCTION

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¹Cognitive and Motor Education Center, Section Of Neurorehabilitation, London, United Kingdom, ²Astrakhan State University, Faculty Of Physical Training And Sports, Astrakhan, Russian Federation, ³Catholic University of Sacred Heart, Department Of Neuroscience, Roma, Italy

Background and Aims:: Several studies have shown that bilateral training in post stroke upper-limb rehabilitation is based on the premise that simultaneous movements of the nonparetic upper limb facilitate performance and recovery of paretic upper-limb function through neural coupling effects. We hypothesized that if we use not only bilateral arm movements but also coordinate and combine them with leg movements, both symmetrically and asymmetrically using motor learning tasks, then this could be the effective strategy for recovering the functionality and motor control of the paretic arm. The aim of the study was to evaluate efficacy of the Upper and Lower Limbs Coordination Training Strategy.

Methods:: Sixty-eight post-stroke (> 6 months) hemiparetic subjects (Brunnstrom recovery stage ≥ 3) were randomly divided into 2 groups: Upper and Lower Limbs Coordination (ULLC) training group (n=36) and Bilateral Upper Limb (BUL) training group (n=32). We proposed the 8-week intervention (5 sessions of 1 hour each, per week). Motor performance was assessed before and after intervention included the Fugl-Meyer assessment (FMA), the Wolf Motor Function Test (WMFT), Box and Block Test.

Results:: In both groups, the tests scores were significantly higher after the intervention, but the ULLC training group demonstrated greater improvement on the FMA test and the WMFT than the BUL training group. All assessments were executed by a blinded evaluator.

Conclusions:: The ULLC training strategy showed to be more effective than BUL training program in recovering the functionality and motor control of the paretic arm in post-stroke (> 6 months) hemi-paretic subjects.
CROSSFIT: A NEUROREHABILITATION PROPOSAL

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Corporación Universitaria Minuto de Dios - UNIMINUTO, Psychology, Bogotá, Colombia

Background and Aims:: CrossFit is a sport practice that generates a healthy and dynamic lifestyle based on functional movements, constantly varied and executed at a high intensity which contributes in multiple areas such as physical and mental health, allowing to potentiate well-being and the physical and mental functioning in relation to activities of the daily living. Objective: Design a rehabilitation program through the practice of CrossFit for people with mild cognitive impairment.

Methods:: A cross-sectional descriptive study, in order to know the neuropsychological functioning of those who do CrossFit and the benefits for those with mild cognitive impairment. Participants were 75 Adults, aged 18 and 60 living in Bogotá, Colombia. Healthy people, who have practice CrossFit for more than 3 months consecutively. A neuropsychological evaluation was required as baseline to know the possible cognitive functions who required attention, finding difficulties in the domain of executive functions (Table 1).

Table 1.
BANFE-2 Scoring system by age range and years of schooling.

<table>
<thead>
<tr>
<th>Participants</th>
<th>Scoring system</th>
<th>Raw Score Mean</th>
<th>Standardized Score Mean</th>
<th>Range Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Subtotal orbitomedial</td>
<td>193</td>
<td>92</td>
<td>Normal</td>
</tr>
<tr>
<td>Group</td>
<td>Anterior prefrontal</td>
<td>17</td>
<td>85</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>subtotal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(16-30)</td>
<td>Dorsolateral Total</td>
<td>204</td>
<td>86</td>
<td>Normal</td>
</tr>
<tr>
<td>(10-24)</td>
<td>Executive function</td>
<td>415</td>
<td>86</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experimental</td>
<td>Subtotal orbitomedial</td>
<td>194</td>
<td>93</td>
<td>Normal</td>
</tr>
<tr>
<td>Group</td>
<td>Anterior prefrontal</td>
<td>18</td>
<td>90</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>subtotal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(16-30)</td>
<td>Dorsolateral Total</td>
<td>234</td>
<td>110</td>
<td>Normal</td>
</tr>
<tr>
<td>(10-24)</td>
<td>Executive function</td>
<td>449</td>
<td>107</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Subtotal orbitomedial</td>
<td>186</td>
<td>87</td>
<td>Normal</td>
</tr>
<tr>
<td>Group</td>
<td>Anterior prefrontal</td>
<td>17</td>
<td>84</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>subtotal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(56-65)</td>
<td>Dorsolateral Total</td>
<td>178</td>
<td>84</td>
<td>Normal</td>
</tr>
<tr>
<td>(10)</td>
<td>Executive function</td>
<td>384</td>
<td>84</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experimental</td>
<td>Subtotal orbitomedial</td>
<td>187</td>
<td>89</td>
<td>Normal</td>
</tr>
<tr>
<td>Group</td>
<td>Anterior prefrontal</td>
<td>17</td>
<td>84</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>subtotal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(56-65)</td>
<td>Dorsolateral Total</td>
<td>180</td>
<td>87</td>
<td>Normal</td>
</tr>
<tr>
<td>(10)</td>
<td>Executive function</td>
<td>385</td>
<td>85</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Note: * Age range, ** Years of schooling

Results:: A neurorehabilitation program was developed addressing two approaches: cognitive-didactic (CrossFit practice) that trains in tasks not very applicable to everyday life and functional-experiential that seeks to recover the ability of people to get involved in activities of daily living focusing on executive functioning (Table 2).
**Table 2**

Neurorehabilitation Proposal based on cognitive functioning and CrossFit

<table>
<thead>
<tr>
<th>Approaches</th>
<th>Tasks to develop</th>
<th>Cognitive subdomains</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Cognitive-didactic</em> (CrossFit practice)</td>
<td>Air squat</td>
<td>Task Initiation</td>
</tr>
<tr>
<td></td>
<td>Pull-up</td>
<td>Self-Monitoring</td>
</tr>
<tr>
<td></td>
<td>Push-up</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Press</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sit-up</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Burpee</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jumping jacks</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lunges</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Knees to Elbows</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Career</td>
<td>Flexible Thinking</td>
</tr>
<tr>
<td></td>
<td>Cycling</td>
<td>Organization</td>
</tr>
<tr>
<td></td>
<td>Rowing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rope Jump (Double Unders)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Box Jump</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wall Balls</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Medicine ball exercises</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Deadlift</td>
<td>Working Memory</td>
</tr>
<tr>
<td></td>
<td>Cleans</td>
<td>Time-management</td>
</tr>
<tr>
<td></td>
<td>Press</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Snatch</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clean y jerk</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kettlebell Swing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bench Press</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Back Squat</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dumbbell</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Front Squat</td>
<td></td>
</tr>
<tr>
<td><em>Functional-experiential</em></td>
<td>Basic activities of daily living</td>
<td>Impulse control</td>
</tr>
<tr>
<td></td>
<td>Instrumental activities of daily living</td>
<td>Decision making</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Planning and Prioritizing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Achieving goals</td>
</tr>
</tbody>
</table>

Note: The hierarchy of intervention according to the neuropsychological evaluation of the pilot study is based primarily on executive functions.

**Conclusions:** People who practice CrossFit at least 3 times a week for more than three months have noticed a favorable change in their health, helping to prevent problems caused by low rates of psychological well-being and quality of life, making this sports practice as a therapeutic alternative to physical and psychological problems related to mild cognitive impairment.
IS TRAINING WITH A FOCUS ON MOTOR LEARNING EFFECTIVE IN IMPROVING BODY COORDINATION IN CHRONIC POST STROKE PATIENTS?

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Background and Aims:: The central tenet in stroke rehabilitation is motor training which includes the interlimb coordination. Several studies robustly demonstrate that the learning of new motor skills is not abolished by stroke. Training of an unfamiliar skill task using either their hemiparetic or non-hemiparetic limbs represents a strategy to improve fine motor function in chronic stroke. We hypothesized that training with a focus on motor learning which includes coordination of all limbs, would be effective in improving motor coordination in patients.

Methods:: Fifty-six post-stroke subjects were recruited. Inclusion criteria: 1) age 40–70 years, 2) unilateral, first ever ischemic stroke more than 6 months before study enrollment, 3) mild to moderate hemiparesis with residual hand function sufficient for task performance, 4) sufficient cognitive function to comply with study requirements. We proposed the 8-week of the complex motor learning intervention (3 sessions of 1 hour each, per week). Motor and functional performance was assessed before and after intervention and included measures of independence in activities of daily living (ADL), the Fugl-Meyer Assessment (FMA), the Wolf Motor Function Test (WMFT), Box and Block Test.

Results:: The motor assessment showed statistically significant improvement in all participants in all the scores tested (t-test performed). The results showed that participants have had the greatest improvements on the FMA test (p < 0.011) and the ADL (p = 0.036).

Conclusions:: Our motor learning training is an effective tool in improving motor coordination and motor control in chronic stroke patients.
COGNITIVE TESTING IN INDIGENOUS POPULATIONS IN CAMEROON – CHALLENGES AND OPPORTUNITIES IN THE BAKA PYGMY AND MBORORO GROUPS

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¹Brain Research Africa Initiative, Neuroscience Research, Yaounde, Cameroon, ²University of Fribourg, Neurosciences, Fribourg, Switzerland, ³c. Neurology Department, Central Hospital Yaoundé/Faculty of Medicine and Biomedical Sciences (FMBS), The University of Yaoundé I, Neurology, Yaoundé, Cameroon, ⁴d. Brain Research Africa Initiative (BRAIN), Yaoundé, Cameroon/Geneva, Switzerland, Administration, Bamenda, Cameroon

Background and Aims:: Cognitive testing is an important method of assessing brain function, in neurological disease. However, indigenous populations with cultural and educational specificities need adapted cognitive assessment tools. This project in the Baka and Mbororo ethnic groups, evaluated the feasibility of using selected cognitive tests from a normalized battery, compared their cognitive performance to urban counterparts and verified the effects of age, gender and education on cognitive performance

Methods:: From 3 indigenous villages in Cameroon, we carried out a community-based, cross-sectional study in 93 healthy children aged 6-16 years to assess fine motor skills and working memory/executive functions using a normalized neuropsychological battery. Demographic, clinical and cognitive data were collected in all participants.

Results:: The mean age was 10.62 years. We obtained descriptive data for cognitive performance per age group in indigenous populations. Large floor effects were observed in 40% of the normalized cognitive tests and thus were not feasible for use in these indigenous groups. Compared to urban children, indigenous children performed significantly better on fine motor assessment tests (p<0.001) and significantly lower on working memory/executive function tests (p<0.001). Applying multiple logistic regression, age and education significantly influenced neurocognitive performance (p<0.001), not gender.

Conclusions:: Our findings support the need for the adaptation of existing and/or development of new cognitive assessment tools integrating the educational, cultural and lifestyle specificities of indigenous groups in Cameroon. This will enhance brain research in these communities with limited access to healthcare and education.
IS LATEROPULSION REALLY RELATED WITH SPECIFIC LESION OF BRAIN?

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Background and Aims:: The lateropulsion (pusher syndrome) is an important barrier to standing and gait after stroke. Although several studies have attempted to elucidate the relationship between brain lesions and the lateropulsion, the effects of specific brain lesions on the development of lateropulsion remain unclear. Thus, the present study investigated the effects of stroke lesion location and size on lateropulsion in right-hemisphere stroke patients.

Methods:: The present retrospective cross-sectional observational study assessed 50 right-hemisphere stroke patients. The lateropulsion was diagnosed and evaluated using the Scale for Contraversive Pushing (SCP). Voxel-based lesion–symptom mapping (VLSM) analysis with 3T-MRI was used to identify the culprit lesion for SCP. We also performed VLSM controlling for lesion volume as a nuisance covariate, in a multivariate model that also controlled for other factors contributing to pusher behavior. VLSM, combined with statistical nonparametric mapping (SnPM), identified the specific region with SCP.

Results:: Lesion size was associated with lateropulsion. The precentral gyrus, postcentral gyrus, inferior frontal gyrus, insula, and sub-gyrual parietal lobe of the right hemisphere seemed to be associated with the lateropulsion, however, after adjusting for lesion volume as a nuisance covariate, no lesion areas were associated with the SCP scores.

Conclusions:: The size of the right hemisphere lesion was the only factor most strongly associated with lateropulsion in patients with stroke. These results may be useful for planning rehabilitation strategies of restoring vertical posture and understanding the pathophysiology of lateropulsion in stroke patients.
TRAUTMATIC AND ISCHEMIC SPINAL CORD INJURIES HAVE A COMPARABLE COURSE OF RECOVERY

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Background and Aims:: The relative rarity of ischemic compared with traumatic spinal cord injury limited comparison of the outcomes of these conditions. Objective. To investigate the neurological and functional recovery of ischemic compared with traumatic acute SCI.

Methods:: Data were derived from the European Multicenter Study Spinal Cord Injury database. Patients with ischemic (iSCI) or traumatic SCI (tSCI), 18 years or older were evaluated at different time points from lesion: 1 month, 3 months, 6 months. The neurological status was assessed at each point by the International Standards for Neurological Classification of Spinal Cord Injury and the functional status by the Spinal Cord Independence Measure. Walking ability was evaluated by Walking Index for Spinal Cord Injury, 10-Meter Walk Test, and 6-Minute Walk Test. Because of the imbalances of the 2 groups in respect to size and lesion severity, a matching procedure according to age, neurological level, and injury severity was performed. Outcomes evaluation was performed by means of a 2-way repeated-measures ANOVA.

Results:: The matching procedure resulted in 191 pairs. Both groups significantly improved from about 15 days after the lesion to 6 months. No differences were found in the course of neurological and functional recovery of iSCI compared with tSCI.

Conclusions:: This analysis from a representative cohort of participants revealed that from 15 days following the lesion, the outcomes after iSCI and tSCI are comparable. This finding supports the potential enrolment of patients with acute iSCI into clinical trials from that point in time after the event and an evaluation up to 6 months afterward.
IMPACT OF THE ONLINE COMPUTER GAME ON 18-24 YEARS OLD YOUNG PEOPLES' VISUAL SCANNING, ATTENTION AND MEMORY

Gokcen Akyurek, Irem Ulukaya
Hacettepe University Faculty of Health Sciences, Occupational Therapy, Ankara, Turkey

Background and Aims:: It is important to consider the potential benefits of games as much as their harms, because the nature of these games has changed dramatically over the last decade, becoming increasingly complex, diverse, realistic, and inherently social. The aim of this study is to compare the visual scanning, attention, and memory functions of young people between the ages of 18-24 according to their playing online computer games (First Person Shooter games).

Methods:: As the research group, fifty computer game players invited from the game site groups and as the control group, fifty participants who are similar age and gender with the research group were included in the study. Multitasking, Visual Search Task, and Corsi Block Test were applied to the participants. Analyzes were made using the Wisconsin test.

Results:: According to the analysis, it was found that there was a statistically significant difference between groups in the Visual Search Task (visual scanning) (p < 0.001). However, there was no statistically significant difference between the groups in Multitasking (attention) and Corsi Block Test (memory) (p > 0.05).

Conclusions:: As a result of this research, it was determined that playing online computer games (First Person Shooter games) has no effect on attention and memory, but on visual scanning. For this reason, it is important to examine this effect by using computer games in addition to the therapy to be applied for individuals with visual scanning problems.
WHAT IS DONE IS NOT ALWAYS WHAT SHOULD BE DONE: RESULTS OF AN ITALIAN SURVEY ON MANAGEMENT OF CRANIOPLASTY IN NEUROREHABILITATION

Fabio La Porta¹, Antonio De Tanti², Anna Estraneo³,⁴, Rita Formisano⁵
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Background and Aims:: Decompressive craniectomy (DC) is often performed in the acute phase of several acute severe Acquired Brain Injuries (sABI) conditions to control intracranial hypertension and reduce mortality. Cranioplasty (CP) is a neurosurgical procedure aiming to reconstruct the skull defect created by DC. While delayed DC may be associated with complications, there may be significant neurological improvements following CP. This work aims to take a snapshot of the management issues regarding DC/CP patients admitted to neurorehabilitation from the Italian Neuro-Rehabilitation Physicians’ (INRP) perspective.

Methods:: The Italian Neurorehabilitation Society Special Interest Group on sABI (SIRN-sABI-SIG) devised a simple questionnaire made of 21 questions. The first 16 explored INRP’s opinions in three main areas (clinical aspects, complications, clinical pathway), whereas the last five questions regarded epidemiological aspects. The survey was then distributed throughout the SIRN-sABI-SIG and other INRP’s mailing lists in April-May 2018.

Results:: The survey was responded to by thirty-eight neurorehabilitation centers, corresponding to 599 patients. Amongst these, the prevalences of DC, CP, and DC+CP were, respectively, 18.9%, 13.5%, and 32.4%. The analyses showed significant differences between INRP’s perceptions about DC/CP management compared to several recommendations of the 2018 International Consensus Conference for CP.

Conclusions:: DC/CP regards about one-third of neurorehabilitation patients in Italy. There is a substantial disagreement between the international recommendations regarding the neurosurgical management of DC/CP (what should be done) and the NPRI’s perception of what is done in practice. Future multicenter and trans-disciplinary prospective studies are warranted to explore and reconcile these controversies.
A FUNCTIONAL BIOMARKER FOR INTERMITTENT HYPOXIA-INDUCED WALKING RECOVERY IN PERSONS WITH CHRONIC SPINAL CORD INJURY

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Background and Aims:: Spinal cord injury (SCI) disrupts connections between the brain, spinal cord, and leg muscles, often causing lifelong walking deficits. Breathing modest bouts of low oxygen (acute intermittent hypoxia, AIH) is a promising strategy to elicit plasticity within spared motor pathways important for restoring walking after SCI. A prior study showed clinically meaningful improvements in walking speed occurred after a single session (D1) that persisted after daily (five consecutive days, D5) AIH in persons with chronic (>1 year), incomplete SCI. Despite the exciting finding, there remains considerable variability in patient responsiveness to AIH treatment. The purpose of this study is to examine the extent to which a single dose-response to AIH may predict long-term response to AIH in persons with SCI.

Methods:: We quantified the dose-dependent associations in walking speed improvements in 19 persons with chronic, motor-incomplete SCI. We computed odds ratios (OR) and 95% confidence intervals (CI) between D1, D5, and 2-weeks follow-up (F2).

Results:: A majority of participants (89.5%) who walked faster at D1 also walked faster at D5 and F2. 60.0±17.5% of participants responded at D1 and F2. Walking improvements at D1 persisted at F2 (OR=10.5; CI=1.1-96.6). The OR increased when associating gains at D5 and F2 (OR=12.0; CI=1.9-75.1).

Conclusions:: Daily AIH shows promise as a treatment to enhance walking function for many but not all persons with chronic, motor-incomplete SCI. Here, we found the early beneficial response to AIH treatment may serve as a functional biomarker for the long-term benefit of AIH treatment after SCI.
RTMS IN PATIENTS WITH ORGANIC AFFECTIVE DISORDER WITH COMORBID PARKINSON'S DISEASE

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Background and Aims: Parkinson's disease, along with motor disorders, involves disorganized neural activity and association with organic affective disorder. Among the first studies performed with rTMS are those with implications in Parkinson's disease and major depression, the aim being the electrical activation of nerve cells and its correlation with increased blood flow in response to rTMS.

Methods: Explaining the results regarding the application of rTMS on 10 case studies that associated organic affective disorder with Parkinson's disease, both diagnoses being medically certified for at least 3 years. The application of rTMS was done 5 times a week in 35-minute sessions for 4 weeks. The measurement of the results was done comparatively by self and hetero-application, Hamilton scale versus Beck scale. In parallel, patients were treated with antidepressant and anti-Parkinson's medication.

Results: Stimulation was done in the left prefrontal cortex considered to be involved in depression. The initial increase in blood flow is followed by a longer period of decreased blood pressure, which stimulates certain functions (learning and memory) that are based on neural activity. Compared to the pharmacologically treated group, scores significantly improved on the motivation scales, self-esteem and subjective perception of quality of life. After 4 weeks, the rTMS group required lower doses of maintenance antidepressant medication.

Conclusions: The rapid change produced by the magnetic impulses that induce depolarization activates at the neuronal level causing the reorganization of the brain through axonal germination. The undamaged axons grow new terminations to fulfill their function.
THE USEFULNESS OF COGNITIVE TRAINING IN ORGANIC AMNESTIC SYNDROME (PATHOLOGY ASSOCIATED WITH ALCOHOLISM - EPILEPSY)

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Background and Aims:: We propose to present the results of a study conducted in the psychiatric clinic on a group of 30 patients diagnosed with chronic alcoholism, who in the first days of hospitalization presented epileptic seizures of grand mal type, later developing various psychiatric pathologies: delirium tremens in the following days, alcoholic psychoses with prolonged evolution, Wernicke Korsakoff type pathology, prolonged organic amnestic syndrome, organic personality disorder, organic affective disorders, mixed dementia (combined ethanolic background + epileptoid).

Methods:: Cerebral neuroimaging, withdrawal treatment, delirium treatment, antiepileptic treatment, neuroprotective, follow-up of GCS, gradual scale of adaptive disability, MMSE, neuropsychological evaluation tests in the area of mnesic prosexial functions and cognition, psychiatric treatment in reality and the retrieval of memories.

Results:: Of the 30 patients investigated, who had prolonged hospitalizations, the average being one month, only 7% developed complicated withdrawal with delirium tremens in the days following epileptic seizures. 75% of those in the study received a diagnosis of the disorder at discharge. organic personality disorder, a quarter of which also associate organic amnestic syndrome. Prolonged alcohol psychosis, which requires the combination of long-term antipsychotic medication, developed in 23% of patients, and in 57% were detected disorders specific to Wernicke Korsakoff syndrome. During hospitalization, a combined pharmacological approach and psychological tests of cognitive recovery were tried.

Conclusions:: Cognitive training related to psychiatric medication (Hasomed battery) ensures the reduction of damage in the area of early Korsakoff-type amnesia, as well as better protection in terms of prevention of prolonged amnestic syndromes or alcoholic psychoses post delirium tremens.
PSYCHIATRIC MORBIDITY AMONG THE PATIENT OF FIRST EVER ISCHAEMIC STROKE

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Background and Aims:: Stroke is the most common cause of mortality worldwide and a serious cause of disability in the community. Stroke affects not only physical but also emotional, psychological, cognitive and social aspects of patients. Some of the neuropsychiatric disorders associated with stroke include post stroke depression (PSD), anxiety disorder, psychotic disorder. Aims and objectives: To evaluate psychiatric morbidity among the patients of first ever ischemic stroke.

Methods:: This cross sectional comparative study was carried out in the Department of Psychiatry, Sylhet MAG Osmani Medical College Hospital, Sylhet during the period from 1st July 2013 to 30th June 2014. Sixty six ischaemic stroke patients of first attack between 2 weeks to 2 years of stroke, aged above 18 years irrespective of sex and 66 accompanying healthy person of the patients and other patients without any kind of stroke matching age and sex fulfilling inclusion and exclusion criteria were taken in Group-A and Group-B respectively. Exclusion criteria were patients with transient ischaemic attack, haemorrhagic stroke, previous stroke, head injury, known psychiatric disorder, serious cognitive impairment and other chronic diseases that may cause psychiatric morbidity.

Results:: Co-morbid psychiatric disorder was found in 23 (34.8%) patients of ischaemic stroke and 9 (13.6%) control subject. The co-morbid psychiatric disorder was significantly higher in patients of ischaemic stroke than that of control subjects (p=0.004).

Conclusions:: Co-morbid psychiatric disorders are quite common among patients with first ever ischaemic stroke in the form of major depressive disorder and generalized anxiety disorder. Therefore, attention should be paid to the anxiety and depressive symptoms in stroke units.
EFFECTS OF PRIMING THERAPIES ON MOTOR IMPAIRMENTS AND IN CORTICAL EXCITABILITY ON STROKE SUBJECTS – SYSTEMATIC REVIEW

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Background and Aims:: Approximately 90% of the subjects with stroke have some type of functional limitation. Priming is an unconscious process associated with learning, in which previous exposure to one stimulus alters the response to another subsequent stimulus. When used successfully in conjunction with another therapeutic intervention, priming can result in a change in behaviour that appears to coincide with changes in neural networks. The aims of this study are to review and to analyse the effects of priming therapies on motor impairments and in cortical excitability on stroke subjects.

Methods:: A bibliographic search was carried out in the databases Pubmed, PEDro and CENTRAL. Only RCT whose intervention explicitly referred to the use of priming therapies, that were performed on subjects who suffered a stroke, were included.

Results:: After applying the eligibility criteria, 14 final studies were included. Of these, 4 used transcranial magnetic stimulation, 3 used transcranial direct current stimulation, 2 used imagery and action observation and 5 used motion-based priming as the main type of priming. Due to the clinical and methodological heterogeneity of the studies, it was not possible the realization of a meta-analysis.

Conclusions:: Of the studies which evaluate the effect of the priming motor recovery, 10 showed that priming associated with rehabilitation had significant improvements and 4 that there were no significant improvements between groups. This review was limited by the small sample of participants, a heterogeneity in methodological and clinical characteristics, only short-term conclusions and lack of consistency in the measured variables between all studies.
“EFFECTIVATE” DIGITAL COGNITIVE TRAINING: A THERAPEUTIC CANDIDATE FOR AGE-RELATED COGNITIVE DECLINE

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Background and Aims:: Even without reaching a pathological threshold, age-related cognitive decline may undermine wellbeing. As life expectancy increases, many individuals are in need of a solution for preserving cognitive abilities. While studies examining the effectiveness of computerized cognitive training showed mixed results, several recent meta-analysis studies concluded there are benefits in cognitive training. In order to address these unmet needs while building upon current findings, we developed "Effectivate", a computerized cognitive training program that focuses on attentional and memory functions. Our objective was to examine the influence of "Effectivate", a self-administered, commercial, cognitive training application, on older adults' attentional and memory functions.

Methods:: Data was collected from 275 "Effectivate" users at two time points, with an average of 52 days between baseline and post-training assessments. During that period, participants could perform one training a day, with a recommendation of 3 training sessions per week. Participants were then divided into 4 subgroups based on their median accumulated training duration and age. Attentional and memory functions were assessed in 4 tasks: processing speed, attentional control, object-location binding and working memory.

Results:: Processing speed task: we found an overall improvement in RTs, which was significantly higher for older participants. Attentional control: a significant Dosage by Assessment interaction was found. Object-location binding: an overall increase in accuracy was found under high visual load. Working memory: Older participants with below-median training dosage showed a decline, while the other subgroups showed no decline.

Conclusions:: These results suggest that the “Effectivate” protocol may support older adults’ cognitive state.
SENSORY-MOTOR AND COGNITIVE IMPROVEMENT BY REINTRODUCING POSTURAL AND BALANCE CONTROL FROM PARETIC BODY SEGMENTS IN STROKE AND TBI PATIENTS

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Background and Aims:: Life after stroke is a key interest in neural rehabilitation. We need an integrating approach that combines the theoretical background of multidisciplinary rehabilitation sciences. Within this worldwide economic situation, every citizen need to give his social contribution to the common welfare. Our pilot study is based on Vasa Concept (VC), developed by Rajul Vasa. VC is a holistic approach to rehabilitate spasticity, motor deficiency, abnormal synergic grouping, subluxation of shoulder, aphasia and neuropsychological symptoms. In comparison with other methods (Beyaert et al., 2015), VC is based on the combination of physiological knowledge of the body functions to neuroscientific findings related to neuroplasticity and brain-derived behaviour. By reintroducing automatic control on local and global center of mass safety to paretic segments, the self-organized brain will recover. Physical and cognitive recovery emerges as by-product. Our aim is to describe in detail the rehabilitation of five patients with neurological symptoms. We also validate the most informative standardized tests for study of a larger patient sample. We will use the results for integrating the study protocol further. The follow-up study will include the evaluations of occupational-, speech-, physiotherapist and neuropsychologist.

Methods:: Standardized tests, measuring upper limb strength and function and balance were performed. Video analysis of motor pre-ambulatory skills and walking was also evaluated.

Results:: Results indicate that VC improves the recovery of motor performance. Significant changes were found in Berg balance test (mean change 4.8 p) and and Hand grip strength (mean change 4.31 kg).

Conclusions:: Pre-walking abilities should be noted more as a base of neurorehabilitation.
THE EFFECTIVENESS OF VIRTUAL REALITY IN THE NEUROREHABILITATION OF CHILDREN WITH HIV-ASSOCIATED NEUROCOGNITIVE DISORDER

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**Background and Aims:** The aim of the study was to evaluate the effectiveness of various neurorehabilitation programs, including the use of memantine hydrochloride and the virtual reality feedback method (NIRVANA) in children with HAND.

**Methods:** The study included 260 children with HIV-positive status and receiving highly active antiretroviral therapy (HAART) according to an individually selected scheme for at least 6 months. All the children included in the study showed signs of HAND. After the initial examination, all patients were divided into 4 groups: only HAART, HAART + memantine, HAART + NIRVANA and HAART + memantine + NIRVANA. The follow-up period was 3 months.

**Results:** In the groups of active neurorehabilitation, there were significant positive changes in the neurocognitive status. As a result, by the end of the 3rd month of follow-up in children taking memantine (HAART group+M and HAART +M+N) achieved a significantly lower IQ score compared to children who were only on HAART (p<0.001 for both comparisons). Also in children who received complex neurorehabilitation (HAART +M+N) by the end of the 3th month of observation, a significantly lower integral score of neurocognitive status assessment was achieved compared to children of the HAART group (p<0.05).

**Conclusions:** Thus, in the course of this study, it was found that children with HAND, despite the ongoing HAART, have a tendency to progress HAND. Children with HIV-associated dementia are most susceptible to progression. The use of active neurorehabilitation, especially a combination of memantine and virtual reality techniques, can significantly improve the indicators of neurocognitive status.
TREATMENT WITH A GAIT DEVICE USING TELEHEALTH DELIVERY IN STROKE SURVIVORS DURING THE CORONAVIRUS PANDEMIC

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Background and Aims:: The coronavirus pandemic prompted healthcare providers to implement strategies to meet patient care needs remotely. This study investigates the feasibility of two adapted telehealth delivery models for remote gait treatment using a novel gait device in chronic stroke survivors.

Methods:: Participants included five individuals with chronic stroke (average age 72 years and 84 months post-stroke). Four of the participants had previously begun in-person treatment with the gait device but had their treatment interrupted by worsening pandemic conditions. These individuals transitioned to the telehealth delivery model to continue their gait treatment remotely. The fifth participant performed all activities (recruitment through follow-up) remotely. The telehealth treatment protocol included a virtual caregiver training session followed by three months of remote treatment with the gait device. To assess feasibility, we monitored safety, compliance, acceptability, and efficacy. Functional improvement was assessed using the 10-Meter Walk Test (10MWT), the Timed Up and Go (TUG) test, and the Six-Minute Walk Test (6MWT) after three months of remote treatment. Sensors were worn during all activities to monitor gait patterns and compliance.

Results:: No significant adverse events occurred and survey responses indicated a high level of acceptability for the remote treatment. Average improvement on the 10MWT, TUG, and 6MWT approached or surpassed twice the minimal clinically important difference or minimal detectable change value. Compliance neared 100% for treatment sessions and assessments.

Conclusions:: The feasibility of safe, remote treatment with the gait device appears promising and could be further evaluated by larger future studies.
EXPLORING THE OPINIONS OF PHYSICAL THERAPIST UNDERGRADUATE STUDENTS REGARDING APPLICABILITY OF TELEREHABILITATION IN STROKE SURVIVORS AND THEIR CAREGIVERS.

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Background and Aims:: Tele-rehabilitation (TeleRehab) is to facilitate rehabilitation procedures for patients suffering from neurological impairments. During this global pandemic, the majority of the Physiotherapists (PT) opted for the TeleRehab mode for their clients to consult and prescribe the protocols. The opinions of the therapists and applicability of TeleRehab in stroke and their primary caregivers have become essential.

Methods:: A qualitative study was designed using an online survey among PT Graduates. A brief structured and validated questionnaire was constructed and sent to PT graduates via What's app and mail.

Results:: The results stated that among n=22 participants, all the participants were familiar with this mode, and they were aware of this through their colleagues, research articles and various social media platforms. About 27% were unaware of its possible use in the Stroke population. A 90% agreed that there are benefits and uses of Tele-rehabilitation, but 81% also agree that this mode comes with several constraints and ethical issues. About 86% felt a prior training is required to use this mode. The major barriers were network connectivity, patient assessment and delivery of treatment.

Conclusions:: The majority of graduate PT noted, Telerehabilitation is a beneficial mode of rehabilitation and also appreciates its advantages and uses.
SARCOPENIA IN PATIENTS WITH NEUROLOGICAL DISORDERS

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**Background and Aims:** Muscular-skeletal disturbances are common in patients with neurological disorders (ND); however, the data about sarcopenia in they are insufficient. The aim was to determine the body composition particularity and sarcopenia frequency in patients with ND (Parkinson's disease (PD), stroke, and spinal cord injury (SCI)).

**Methods:** 410 subjects aged 23-79 years were included, being divided into two groups: the group of healthy subjects (group I, n=160) and a group of patients with ND (group II, n=250 (89 PD patients, 84 stroke patients, and 77 SCI subjects)). Body composition was measured using dual-energy X-ray absorptiometry. Sarcopenia was diagnosed according to the appendicular lean mass index (< 7.2 kg/m² for men and < 5.45 kg/m² for women).

**Results:** Sarcopenia had not been reported in PD patients. We did not find any significant differences in their lean mass index, however, the fat mass index in PD patients was probably lower – 18.4%. The lean mass was significantly lower in stroke patients than in group I, however, the fat mass did not differ significantly. The frequency of sarcopenia in stroke patients was 16.7%, among SCI subjects – 84.3% versus 6.5% in group I (p<0.0001), but their fat mass, on the contrary, was higher.

**Conclusions:** The study did not show common features of body composition for patients with neurological disorders. Sarcopenia is significantly more common in SCI persons and stroke patients, however, is not registered in subjects with PD. On the contrary, fat mass significantly lower in PD patients and higher in stroke and SCI subjects.
REPEETITIVE TRANSCRANIAL MAGNETIC CORTICAL STIMULATION FOR RESISTANCE DIABETIC NEUROPATHIC PAIN

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Background and Aims:: No single treatment exists to prevent or reverse neuropathic changes or to provide total pain relief. Although medical treatment are useful, they produce a diversity of side effects and are occasionally ineffective. Repetitive transcranial magnetic stimulation (rTMS) safe, non-invasive and effective therapeutic opportunities for many neurogenic disorders. This study was designed to assess the efficacy rTMS for treatment resistance neuropathic pain (NP) in diabetic patients.

Methods:: forty six subjects had resistance NP, were divided equally real rTMS and sham rTMS. The NP level was scored on a visual analogue scale before and after a 20 sessions, each session had 20 minute 10 Hz rTMS over the side of the motor cortex corresponding to the on the painful side.

Results:: The percentage NP reduction was significantly greater real rTMS than sham rTMS, confirming that motor cortex rTMS was able to induce antalgic effects. These effects were significantly influenced by the origin and the site of pain. Across representation plasticity of cortical areas resulting from deafferentation could explain this discrepancy.

Conclusions:: Motor cortex rTMS achieved significant short-term pain relief of the NP.
HEMATOCRIT CHANGES DURING EARLY POST-STROKE REHABILITATION WITH ORAL HYDRATION AND WITHOUT

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Background and Aims:: General blood test is the simplest and most accessible method of research, which provides sufficient information about the body. We aimed to find out if water consumption during the early rehabilitation stage can impact the blood hematocrit(HTC) level in patients with stroke.

Methods:: A total of 214 stroke patients were included, attending the early stage of rehabilitation program that consist of kinesitherapy and mechanotherapy daily. For each participant blood test was performed 15 minutes before and 10 minutes after session. The duration and intensity of physical activity were adjusted individually. During training 107 patients drank water and 107 did not.

Results:: We found differences between two groups. HTC level in water consumption group changed from 60.33% before exercise to 54.56% after, so it decreased by 5.77%. However, patients who did not drink water showed HTC increasing: 59.71% before exercise and 61.12%, therefore increased by 1.41%.

Conclusions:: Elevated hematocrit adversely affects the blood rheological properties, increasing the risk of thrombosis and recurrence of stroke. Therefore, drinking enough water is one of the key factors not only in rehabilitation improvement, but also in the prevention of unexpected complications.
MARCHIAFAVA-BIGNAMI DISEASE PRESENTING AS MIXED TRANSCORTICAL APHASIA.

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Background and Aims:: Marchiafava-Bignami disease (MBD) is a rare demyelinating and necrotic disorder of the corpus callosum, classically presenting with altered mental status. Increasing evidence shows that lesions can localize also in the subcortical white matter, presenting with focal symptoms and carrying a poorer prognosis. We describe the clinical and radiological findings of a patient with MBD presenting as mixed transcortical aphasia (MTA), remarkably improving after thiamine treatment.

Methods:: A 48-year-old male was admitted to our emergency department with clinical suspicion of stroke for the acute onset of aphasia. He had a 30-year history of alcohol abuse and recent poor feeding. He was slowed down on psychomotor level, confused, disoriented in time, space and on personal information. Neuropsychological evaluation revealed frontal lobe dysfunction and a marked language disturbance fitting the diagnosis of MTA. MRI showed marked diffusivity restriction in the corpus callosum, mainly in the splenium, and in the subcortical left fronto-parietal and occipito-temporal white matter, suggesting the diagnosis of MBD.

Results:: After treatment with high dose Thiamine we documented a definite improvement of his mental status and a partial regression of the callosal signal alteration, while aphasia persisted.

Conclusions:: To our knowledge, this is the first case of MBD presenting as MTA, a rare entity usually caused by infarctions that disconnect the left perisylvian area, thus sparing the arcuate fasciculum, Wernicke and Broca area. Focal symptoms at onset may sometimes delay the diagnosis of this treatable condition. We recommend considering MBD in the differential diagnosis of patients with malnutrition and alcoholism, independently from clinical presentation.
“CHASING THE DRAGON”: A RARE LEUKOENCEPHALOPATHY DUE TO HEROIN INHALATION TOXICITY

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Background and Aims:: Leukoencephalopathy due to heroin inhalation toxicity is a white matter disease, with an unclear aetiology, characterized by symmetric spongiform degeneration. The patients may progress through three defined clinical stages that could lead to death.

Methods:: Last year, in September, a 52 years-old patient with decreased level of consciousness and spastic quadriparesis occurred to our Emergency Department. Since her childhood she was drugs addict and few months before she required hospitalization for heroin abuse. She presented fever and she underwent an EEG (with interictal epileptiform discharges) and a lumbar puncture hypothesizing an encephalitic syndrome but chemical, bacteriological and virological exams were normal. A first CT scan was negative. Suspecting a catatonic state she was treated with high dose of Lorazepam without clinical results. During the hospitalization, she underwent a brain MRI that revealed symmetric hyperintensities on T2 weighted sequences involving cerebral white matter (particularly posteriorly), corticospinal tract and sparing of the subcortical white matter. We introduced baclofen, ubiquinone and vitamins supplement.

The patient’s condition slowly deteriorated because of vegetative seizures, treated with Lacosamide.
Results: For a month, she was aphasic and she layed in bed. After a long period of rehabilitation she walks with bilateral assistance and she pronounces simple sentences. At discharge time, she was still dysphagic and she needed a PEG (percutaneous endoscopic gastrostomy) to feed herself.

Conclusions: Although the heroin inhalation is not a frequent current practice, we should suspect toxic leukoencephalopathy when a “drugs addict” patient is admitted to the hospital for sudden decreased levels of consciousness.
B12 DEFICIENCY PRESENTING AS SENSORY NEURONOPATHY

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Background and Aims: Vitamin B12 deficiency is a common but underdiagnosed condition and has protean manifestations affecting both central and peripheral nervous systems. Sensory ganglionopathy due to vitamin b12 deficiency is a seldom described but easily treatable condition which should be always be a part of the etiological differential diagnoses.

Methods: We describe 3 patients who presented with subacute onset of painful paresthesias over the feet followed by face, hands, with h/o wash basin ataxia, imbalance while walking. Clinical examination revealed impaired joint position, vibration, positive romberg’s test, asymmetric loss of pain, crude touch over hands and limbs, diffuse areflexia. 1st had knuckle hyperpigmentation, 2nd had familial premature greying of hair, 3rd was a daily alcohol abuser. Clinical diagnosis of sensory ataxia was made and evaluated.

Results: Investigations revealed raised MCV, low serum b12 levels, hyperhomocysteinemia. All 3 patients being omnivorous, search for etiology revealed positive Anti parietal cell antibodies in 2 patients. Electrophysiological study was s/o severe, asymmetrical, non length dependent sensory action potential attenuation with normal motor conduction parameters suggestive of possible sensory neuronopathy as per published diagnostic criteria. We ruled out classical causes of sensory neuronopathy. The patients received injection B12 and folate replacement. All patients showed remarkable improvement in both clinical and electrophysiological parameters at 3 month follow up.
Conclusions:: 50% of patients of sensory ganglionopathy are labelled idiopathic after evaluation of established causes. Vitamin B12 deficiency should be systematically ruled out even in omnivorous as this is an easily remediable & therapeutically rewarding cause of sensory neuronopathy.
RIBOFLAVIN IN NEUROLOGICAL DISEASES

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Background and Aims:: Accumulating evidence suggests that riboflavin has multiple effects on several cellular pathways, some of them relevant for mechanisms of neurodegeneration, shared by the main neurological diseases. In this review of the literature we analyze the therapeutic effects of riboflavin on the pathogenesis of different neurological diseases.

Methods:: To select the relevant literature for this narrative reviews the authors searched pubmed and google scholar databases as well as their personal article libraries using the following string: “Riboflavin” AND (“neurology” or “nervous system” or “myelin” or “brain” or “peripheral nervous system” or “neuropathology” or “deficiency”). Articles in languages different than English, published before the 1960s or reported only as abstracts were not considered suitable and were discarded.

Results:: Several successful trials testing riboflavin for migraine prevention were performed and this drug is currently classified as a Level B medication for migraine according to the American Academy of Neurology evidence-based rating. Brown-Vialletto-Van Laere syndrome and Fazio-Londe disease are now renamed as “riboflavin transporter deficiency”, because these are autosomal recessive diseases caused by mutations of SLC52A2 and SLC52A3 genes that encode riboflavin transporters. High doses of riboflavin represent the mainstay of the therapy of these diseases. Some mitochondrial diseases respond to supplementation with riboflavin. These include multiple acylCoA dehydrogenase deficiency (which is caused by ETFDH gene mutations in the majority of the cases), mutations of ACAD9 gene, mutations of AIFM1 gene, mutations of the NDUFV1 and NDUFV2 genes.

Conclusions:: Future studies need to elucidate whether and how riboflavin may be used as an add-on treatment in many neurological diseases.
CENTRAL PONTINE MYELINOLYSIS AS A CONSEQUENCE OF HYPEREMESIS GRAVIDARUM: A CASE REPORT.

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Background and Aims: Few cases of central pontine mielinolysis (CPM) are reported in the literature, mainly linked to hyperemesis gravidarum which may cause incorrect absorption of thiamine. In this report we described the case of CPM in a 17 weeks pregnant woman with hyperemesis gravidarum.

Methods: The patient underwent neurological examination which disclosed the hallmarks of a cerebellar syndrome (dysarthria, horizontal nystagmus, bilateral dysmetria, positive Romberg sign, abasia, gait disorder) and a paretic syndrome with mild piramidal signs (asymetric reflexes of lower limbs and inexhaustible Achilles clonus). No disturbaces in electrolytes were reported in previous routine pregnancy controls, whereas a severe recent weight loss merged. No history of alcol or drug abuse emerged.

Results: Initial laboratory tests showed moderate anemia and hypoglicaemia, without alteration of electronitical balance. Admitted with a CT scan showing central-pontine hypodensity, a subsequent brain MRI highlighted a pontine-centred focal signal alteration, hypointense in T1-weighted sequences, hyperintense in T2-weighted (FLAIR) sequences, with a diffusion restriction on diffusion-weighted images and increased ADC values. Radiological pattern matched features of CPM. According to the anamnestic and laboratory findings, a diagnosis of CMP due to Wernicke’s encephalopathy was made. Tiamine was administrated (500 mg/3 times/day for two days, then 250 mg/2 times/day) with an improvement of symptoms and neurological signs.

Conclusions: CPM in pregnancy is a rare but not negligible neurological complication, requiring a prompt intervention. While its occuring in isolation is not typical for Wernicke’s encephalopathy, this etiology should be taken into account in the differential diagnosis of suspected metabolic encephalopathy.
HEROIN INDUCED ACUTE MYELOPATHY, Rhabdomyolysis AND CHRONIC GLOBUS PALLIDUS ISCHEMIA: UNCOMMON COMPLICATIONS OF HEROIN ABUSE

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Background and Aims:: Heroin or diacetylmorphine is widely consumed illegal opioid. Neurological manifestations of heroin include Spongiform lekoencephalopathy, ischemia, botulism, myelopathy, neuropathy and cerebral atrophy. Heroin myelopathy is a very rare manifestation seen in relation to first episode of heroin usage or following consumption after a period of abstinence. Neurovascular ischemia is the most common complication involving Globus pallidus, periventricular and subcortical regions. We describe a rare case of acute myelopathy, rhabdomyolysis and Globus pallidus ischemia in a chronic heroin user.

Methods:: A 41 year old Sri Lankan man presented with acute bilateral lower limb weakness, numbness and urinary retention followed by unconsciousness four hours after using inhaled heroin. He has consumed heroin after two years of abstinence. Examination revealed flaccid paraparesis with a sensory level at T7. Joint position senses were absent.

Results::

Haematology was abnormal with very high CPK (10431 U/L), hyponatremia (128 mmol/l), high creatinine (13.2 mg/dl) and positive urine myoglobin. MRI spine showed T2 FLAIR hyperintensities in cervical region involving anterior and central cord. There were T2 hypo intensities in Globus Pallidus with a central hyperintensity, mimicking a ‘tiger’s eye appearance’ along with contrast enhancement and blooming artifacts in SWI. T2 hyper intensities were noted in paraspinal muscles due to rhabdomyolysis. Heroin induced acute myelopathy was diagnosed along with rhabdomyolysis and kidney injury. Patient improved with hemodialysis and methylprednisolone pulse.
**Conclusions:**

Suggested mechanisms of acute heroin myelopathy include direct toxicity, hypersensitivity, vasculitis and hypotension. Globus Pallidus is the commonest brain structure to be affected in 5-10% of chronic heroin users.

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**Figure 01:** T2, FLAIR hyperintensities in C2/3, C4/5 and C5/6 regions
Extra-pontine Osmotic Demyelination Syndrome and Membranous Nephropathy

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Background and Aims:: Rapid correction of hyponatremia can increase the risk of osmotic demyelination syndrome (ODS) involving the central pons and extrapontine (basal ganglia) brain areas. We described a patient who developed extrapontine ODS after rapid correction of profound hyponatremia in the setting of severe nephrotic syndrome (NS).

Methods:: Case Description:
A 45 years old male, previously healthy, presented with 8 days history of ataxia, slurred speech, vomiting and confusion. Laboratory showed severe electrolyte imbalances including profound symptomatic hypotonic hyponatremia of 96 mmol/l, hypokalemia (K : 2.1 mmol/l), with normal creatinine level and severe mixed alkalosis. He received hypertonic saline and fluids with rapid correction of hyponatremia to 124 within 24 hours. He also had hypoalbuminemia (10 g/l), massive proteinuria and mixed hyperlipidemia. Kidney biopsy revealed membranous nephropathy and secondary focal and segmental glomerulosclerosis with positive PLA2R-Ab. He was treated with Tacrolimus, prednisolone and atorvastatin. Two weeks later, he developed dysphagia, confusion and ataxia and MRI brain showed extra-pontine osmotic myelinosis. He required nasogastric tube for feeding and physiotherapy with gradual clinical improvement.

Results:: Discussion:
Conditions associated with increased risk of ODS include alcoholism, malnutrition, symptomatic hyponatremia below 105 mmol/l, liver disease and hypokalemia. The association of extrapontine myelinosis and nephrotic syndrome has been reported in a 6 years old girl. Our patient was diagnosed with primary membranous nephropathy and had other risks factors for developing ODS.

Conclusions:: Extrapontine myelinosis resulted from rapid correction of profound hyponatremia and hypokalemia. Severe nephrotic syndrome related to membranous nephropathy might be considered as a potential risk factor for ODS.
NON-ALCOHOLIC WERNICKE’S ENCEPHALOPATHY WITH ATYPICAL BRAIN MRI IN SETTING OF SEVERE SUBACUTE MALNUTRITION

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Background and Aims:: Wernicke encephalopathy (WE) classically presents as encephalopathy, oculomotor dysfunction, and gait ataxia. WE usually occurs in the setting of chronic alcohol use and thiamine insufficiency. MRI imaging generally demonstrates edema of the periaqueductal region of the midbrain, mammillary bodies, and thalamus. Basal ganglia (BG) involvement, more commonly seen in pediatric WE, is classically thought to differentiate pediatric versus adult WE. However, we report a case of adult non-alcoholic WE with both thalamic and BG involvement.

Methods:: A 73-year-old woman with a past medical history of hypertension, diabetes mellitus, and unintentional 40 lbs weight loss presented with a chief complaint of acute onset double vision and gait instability. The patient underwent a recent esophagogastroduodenoscopy demonstrating a gastric mass leading to poor oral intake. The patient denied any alcohol use.

Results:: Neurologic examination was significant for bradyphrenia and bilateral ophthalmoplegia including inability to abduct with either eye as well as bilateral vertical nystagmus on upward gaze. Ataxic gait was noted. Laboratory examination showed low thiamine levels of 32nmol/L (ref 78-185nmol/L). MRI brain showed multifocal bilateral areas of old infarcts, diffusion restriction involving the bilateral medial thalami with abnormal FLAIR signal involving the basal ganglia bilaterally. Overall presentation was suggestive of atypical WE. Patient was treated with high-dose IV thiamine followed by oral supplementation.

Conclusions:: WE may present in cases of severe subacute malnutrition and poor absorption even in the absence of alcohol use. Although imaging with BG involvement is atypical in adults, this should not rule out WE if clinical presentation strongly suggests WE.
NEW PRESENTATION ON PILOCYSTIC ASTROCYTOMA (PA): A DISCUSSION FOR MECHANISMS OF DEATH

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Background and Aims:: The most common causes of sudden unexpected death are cardiovascular diseases, followed by central nervous system (CNS), and respiratory and gastrointestinal diseases. Sudden death in persons with intracranial neoplasms is a rare mechanism of death detected in the forensic autopsies. Among the deaths due to intracranial neoplasms, sudden deaths due to polycystic astrocytoma (PA) are rarely reported in literature. In this case-report we discuss rare autopsy case of Pilocystic astrocytoma with unusual severe emaciation who was died from myocarditis.

Methods:: Full forensic examination of the body was performed with subsequent chemical and histological analysis.

Results:: Autopsy findings showed a small, solid cerebellar mass without any bleedings which was located on third ventricle brain and attached in choroid plexus. Histological diagnosis was PA, low-grade tumor. A slight accumulation of lipofushin pigments in the cytoplasm of myocytes, a focal chronic inflammatory cells infiltration predominantly lymphocytes with changes on degenerative on other myocytes were also seen in the heart.

Conclusions:: Rare cause of profound emaciation is tumores affecting the diencephalon. The clinical presentation may differ, depending on the location of the lesion and age of the patient. We hypothesize that PA induce generalized cachetic in a paraneoplastic fashion either by formation of antiadipocyte autoantibodies. In addition of, there is an unknown way to starting of myocarditis. We conclude that the diagnosis of brain tumor should be considered in young children presenting with generalized and severe unexplained cachexia with or without metabolic abnormalities. Forensic pathologists must keep in mind that sudden unexpected death caused by intracranial meningiomas, although extremely rare, may be encountered in the forensic setting.
PARKINSONISM AND CORTICOSPINAL TRACTS INVOLVEMENT IN HEPATIC ENCEPHALOPATHY

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Background and Aims:: Hepatic encephalopathy (HE) is characterized by cognitive, psychomotor and psychiatric symptoms due to liver failure and/or portal-systemic blood-shunting. Pathophysiology of HE is multifactorial, partially caused by brain accumulation of ammonia and other metabolites. Manganese is thought to be responsible of development of parkinsonism with typical bilateral symmetric T1-hyperintensity of basal ganglia at brain MRI. Moreover, T1-signal changes of white matter had been reported, but its clinical relevance is still debated.

Methods:: A 67-year-old male with exotossic cirrhosis, resolved HBV infection and history of HE in hyperammonemia developed acute lethargy, amnesia, disorientation in time and space and dysarthria since about 48 hours. Neurological examination showed diffuse hypo-elicitable reflexes, asterixis, postural and telekinetic tremor, dysmetria and mild rigidity at both upper limbs. He underwent blood analysis, EEG and brain MRI.

Results:: Ammonia was 97 μmol/l (normal range 21-50 μmol/l). EEG was unremarkable, while brain MRI showed bilateral T1-hyperintensity of substantia nigra, globus pallidus, posterior limb of internal capsules and corticospinal tracts. Diagnosis of HE was made. Treatment with hydration, branched-chain polyaminoacids, lactulose and rifaximin induced cognitive and motor improvement.

Conclusions:: Manganese accumulation in basal ganglia with development of parkinsonism in HE patients is well known. Manganese acts as neuronal MRI contrast agent: its ion (Mn\textsuperscript{2+}) is taken-up into intracellular space and diffuses throughout cytoplasm and axons transported by microtubules. Our findings of corticospinal tracts T1-hyperintensity could suggest manganese deposition in these structures too, even if no pyramidal sign was evident. Surely, this condition deserves a longer follow-up to detect potential long-term effects.
WERNICKE ENCEPHALOPATHY SECONDARY TO HYPEREMESIS GRAVIDARUM: THIRD LEVEL HOSPITAL EXPERIENCE

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Background and Aims:: Vitamin B1 (thiamine) deficiency causes an acute neurological condition known as Wernicke encephalopathy (WE). In the developed world, WE is usually secondary to alcoholism. In some cases it may be secondary to hyperemesis gravidarum (HEG). In this paper, we report 5 cases of Wernicke’s encephalopathy secondary to hyperemesis gravidarum. Our aim is to highlight the importance of thiamine supplementation in cases of prolonged vomiting during pregnancy.

Methods:: We collected retrospectively the observations of all patients with Wernicke encephalopathy (WE) hospitalized in the Department of Neurology (Mohammed VI university hospital, Marrakech) during a period of 2 years (between September 2018 and September 2020). Each patient had benefited from magnetic resonance imaging of the brain (MRI) with venography, vitamin B1 screening was unavailable.

Results:: We found 5 cases of WE secondary to HEG, two of the five women were primi-gravidae, the mean age was 25.8 years. all the five women were non-alcoholic. One patient had hypothyroidism and had developed WE in her previous pregnancy, another one had depression. All the five patients had developed intractable vomiting early on in the first trimester. They all had a decreased level of consciousness, ataxia with concomitant dry beriberi.

Conclusions:: In countries, where religion forbids the consumption of alcohol, hyperemesis gravidarum (HG) may be the main cause of thiamine deficiency, consequently leading to WE. It is important to consider thiamine supplementation in cases of hyperemesis gravidarum or prolonged vomiting in pregnancy. A timely diagnosis of WE in pregnancy is important and its prevention in subsequent pregnancies is mandatory.
ANALYSIS OF THE TROPHIC STATUS OF PATIENTS WITH CORONAVIRUS DISEASE COMPLICATED BY CAVERNOUS SINUS THROMBOSIS.

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Background and Aims:: It is known that Covid-19 disease is severe in obese and elderly people. The study once again proves the high risk of complications in these patients. Identification of risk factors based on an assessment of the trophic status of patients complicated by cavernous sinus thrombosis.

Methods:: In the multidisciplinary clinic of the Tashkent Medical Academy, in 36 patients with Postcovid syndrome complicated by thrombosis of the cavernous sinus. The average age of the patients was 60 ± 8 years, of which 26 women (57.8%) and 19 men (42.2%). All patients underwent an bioimpedancometry (Tanita BS-585, Japan)

Results:: Deviations from the ideal body weight were found in 87% of cases, body weight deficiency was noted in 14% of patients, an increase in adipose tissue mass in 73% of patients. The average values of the indicator of total and visceral fat mass were 23% higher than their characteristic physiological norm, lack of muscle mass from 13-25 kg was revealed. The total percentage of water in the body varied from 35 to 65%, since in overweight patients below normal - 42.2 ± 2.12 (p≤0.01). The calculated indicator of basal metabolism on average corresponded to 1 995.1 ± 50.34 kcal, which is 18% lower than the required value, but indicates a reduced physical activity

Conclusions:: According to bioimpedancemetric analyzes, the deviation of many indicators of the composition components of the body was interpreted, as it means a violation of the physical, metabolic status. Such patients have a high risk of complications, unfavorable outcome of the underlying disease.
CONCOMITANT HIGH OXIDATIVE STRESS AND POOR ANTIOXIDANT ENZYME ACTIVITY WITH DNA DAMAGE MAY UNDERLIE OBESITY AND REDUCED LONGEVITY IN WNIN/OB OBESE RATS

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Background and Aims:: Disequilibrium between the production of reactive oxygen and ability of an organism to readily detoxify the reactive intermediates or easily repair the resulting damage is termed as oxidative stress (OS). OS is believed to be involved in development of various pathologies like Alzheimer’s disease, cancer, accelerated aging and many others. On the other hand, OS itself arises from medical conditions like obesity. Wistar of National Institute of Nutrition Obese (WNIN/Ob) obese rats are the novel rat models presenting a link between obesity and ageing.

Methods:: We evaluated the oxidative stress parameters, C-reactive protein levels, DNA damage status and astroglial infiltration in the different brain regions.

Results:: Our studies clearly show the progression of OS and accumulation of DNA damage in brain at an early age causing accelerated aging in these rat models. Imbalance in the levels of trophic factors IGF1 and BDNF, both in plasma and brain, implies altered signaling which in turn leads to hyperphagic behavior and stress. The increased C-reactive protein levels and astroglial infiltration further give clues regarding increased cellular stress and damage in important brain areas like hypothalamus, hippocampus and cerebral cortex.

Conclusions:: Here the link between obesity and brain aging has been proposed with future directions of research. Ethical Statement: This study was performed in accordance with the protocols duly approved by the institutional animal ethical committee. Source of funding: Indian Council of Medical Research, New Delhi.
Background and Aims:: The neurological manifestations of celiac disease (CD) are rare, polymorphic and often severe. They can inaugurate the disease in 9.4% of CD. Our Aim is to illustrate this polymorphism via a case report and to approve that The gluten-free only improves peripheral lesions in the majority of cases while the central-lesions progress on their own.

Methods:: We present the case of a patient with CD and followed for mixed involvement of the central and peripheral nervous system.

Results:: Our patient is 55 years old, with CD, discovered 20 years ago, on a gluten-free diet badly observed. She presented with gait instability that is progressively worsening since 3 years. Neurological examination showed a static and kinetic cerebellar syndrome, a posterior cord syndrome and bone tendon reflexes abolished in the 2 lower limbs. The cytochemical analysis of the cerebrospinal fluid was normal. Absence of an oligoclonal band in the CSF. Thyroid analysis as well as the dosage of vitamins B12 and B1 were normal. The immunological analysis was negative (ANA, anti-intrinsic factor and anti-parietal cell antibodies). VS = 10, Electromyogram: sensory axonal neuropathy. Cerebral and spinal MRI showed a right temporal hypersignal, diffuse pontic and cerebellar atrophy. The patient was put on vitamin therapy in combination with a well-managed Gluten-free diet. We note only the amelioration of her neuropathy after 3 months with regular diet.
Conclusions: Cerebellar ataxia and peripheral axonal-sensory-neuropathy are the common neurological damage in CD. Cerebellar atrophy was proportional to the disease progression. The diagnosis should only be made after ruling out other differential-diagnoses.
A 60 DEGREE CELCIUS OF GASSERIAN GANGLION ABLATION WITH IMPROVEMENT ON PSORIASIS PATIENT WITH TRIGEMINAL NEURALGIA: A CASE REPORT

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Background and Aims:: Scalp psoriasis is a chronic disease found in 45% to 58% of patients, while neuropathic symptoms are found in 26% to 56.3%. TN requires long-term treatment, and RFA is a treatment with satisfying improvement.

Methods:: A male, 39 years old, with right hemifacial pain (NRS 6-8) for 3 weeks, that corresponded to all branches of the trigeminal nerve. No head-face trauma was experienced, and since 2008 suffered from scalp-psoriasis. Brain MRI observed normally, while 3D Fiesta with right SCA and TN contacted (3.5 mm from the entry zone). Carbamazepine 600 mg and amitryptiline 25 mg were prescribed without improvement. Insertion of a 15 mm RF insulated needle was placed in Meckel's cavity after the local anesthetic, a single cycle of 60° C and 90 seconds is set after branches are confirmed together. A 0.2 mL of 10 mg triamcinolone injected gently before pulling out.

Results:: Clinical improvement on week 2 (NRS 2-3), and week 16 (NRS 0-1). Pain and itch are sensed by C-fibers of the DRG and trigeminal ganglion. Psoriasis might increase SP and CGRP, so lead to central trigeminal ganglion and peripheral sensitization.

GENETIC STUDY OF ITALIAN FAMILIES AFFECTED BY SMALL FIBRE NEUROPATHY IDENTIFIED VARIANTS IN PREDISPOSING PAIN PHENOTYPE

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Background and Aims:: Peripheral Neuropathy (PN) affects 2.4% of people and almost 50% of general population is known to have pain-related symptoms. Genetic studies in painful PN (PPN) revealed that Voltage Gated Sodium Channels (VGSCs) genes are involved in pain amplification. Here we aimed to broaden the genetic aspect of PPN by using whole exome sequencing (WES).

Methods:: Six families with PPN were selected having at least one affected member, positive neurological examination and pain questionnaire result with numerical rating score ≥ 4. Variants were filtered with a manually curated gene panel, allele frequency (AF) and computational predictors. Segregation causative/protective models were applied according to pedigree and sharing models were applied after grouping probands of each family.

Results:: According to segregation causative and protective model, we found 129 and 112 variants respectively (AF≤10%) across families. Among genes shared between two families with causative approach, variants were observed in SCN9A, SV2C and DST, whereas protective variants in TRPM2 and LRP1. In shared model, we identified 21 variants and 53 genes shared across ≥ 3 probands. Among shared genes with predicted high-impact variants in probands were observed in SCN9A, SCN7A, P2RY4, P2RX7, TRPV4 and TRPM1.

Conclusions:: WES approach appears powerful in mutation detection and in revealing new genotype-phenotype association. In addition to VGSCs, other gene families including Transient Receptor Potential and Purinergic Receptor seem to play a role in pain modulation. The same approach will be replicated on new families already sequenced before proceeding with ad hoc functional experiments to deepen the role of genes in painful phenotype.
NEEDLE PHOBIA AND PAIN AMONG ELECTRODIAGNOSTIC SUBJECTS: PRELIMINARY SURVEY.

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Background and Aims: Needle phobia, otherwise known as trypanophobia, is seen in at least 10% of the general population. We evaluated the effect of needle phobia on the perceived and actual pain during electrodiagnostic procedures in this study.

Methods: Prospective subjects referred to our electrodiagnostic laboratory between July and August 2020 were interviewed. Demographic data, perceived pain score (using a visual analogue scale) for nerve conduction test (NCT) and electromyography were assessed. Needle phobia score (using a needle phobia scale) was collated and analyzed.

Results: Of the 38 subjects, 24 were male and 14 were females with mean age of 43.11±12.2 and 41.05±16.83 respectively (p=0.662). The needle phobia score was not different between female (13.25±15.43) and males (17.40±11.63), p=0.56. The mean perceived pain score for NCT was 4.73±2.93 while mean of actual pain score was 4.94±2.33 (p=0.028). The mean perceived pain score for EMG was 2.69±2.24 while mean post score was 4.25±3.31, (p=0.028). There was a direct correlation between pre and post NCT pain scores (correlation coefficient 0.457, p=0.007) and pre-EMG and post EMG pain scores (correlation c=0.558, p= 0.025). Trypanophobia index was positively correlated to the perceived pain but not actual pain on EMG.

Conclusions: Inquiry about needle phobia and treating them may ensure more cooperation and tolerability of electrodiagnostic procedure, especially electromyogram in high-risk subjects.
Background and Aims:: it is well known that brain derived neurotrophic factor (BDNF) can modulate pain symptoms in diabetic polyneuropathy (DPN). It is still not known which type of receptor mediates its hyperalgesic effects. Aim: to compare serum levels of BDNF and tropomyosin receptor kinase type B (trkB) in patients with a painful and painless forms DPN.

Methods:: we studied 56 patients with DPN divided into two groups: the 1st group of 30 patients with neuropathic pain, and the 2nd group of 26 patients without pain symptoms. Pain intensity was examined by PainDetect. Presence of DPN were assessed by neurological examination according to the Michigan neuropathy screening instrument (MNSI) and electroneuromiography (ENMG) of lower extremities. Serum levels of BDNF and TrkB were studied by enzyme immunoassay.

Results:: The comparison of clinical and ENMG data for both groups is presented in Figure 1.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>U-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>61.00±9.82</td>
<td>58.90±10.78</td>
<td>0.882</td>
<td>0.377</td>
</tr>
<tr>
<td>Duration of DM, years</td>
<td>12.00±6.39</td>
<td>14.08±6.10</td>
<td>-0.753</td>
<td>0.223</td>
</tr>
<tr>
<td>Fasting blood glucose level, mmol/l</td>
<td>11.09±2.84</td>
<td>12.72±3.64</td>
<td>-0.844</td>
<td>0.519</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>8.97±2.04</td>
<td>9.9±1.91</td>
<td>-0.788</td>
<td>0.078</td>
</tr>
<tr>
<td>PainDetect</td>
<td>23.11±7.65</td>
<td>7.63±6.15</td>
<td>3.064</td>
<td>0.002</td>
</tr>
<tr>
<td>MNSI</td>
<td>4.52±2.83</td>
<td>5.9±2.58</td>
<td>-0.862</td>
<td>0.163</td>
</tr>
<tr>
<td>M-amplitude, mV</td>
<td>1.23±1.57</td>
<td>1.01±0.91</td>
<td>0.282</td>
<td>0.277</td>
</tr>
<tr>
<td>Latency M-amplitude, mc</td>
<td>4.52±1.3</td>
<td>4.87±1.97</td>
<td>-0.965</td>
<td>0.168</td>
</tr>
<tr>
<td>NCV, n. peroneus, m/s</td>
<td>21.33±5.95</td>
<td>23.17±6.47</td>
<td>-0.162</td>
<td>0.421</td>
</tr>
<tr>
<td>S-amplitude, mV</td>
<td>1.39±0.96</td>
<td>1.62±0.83</td>
<td>-0.892</td>
<td>0.382</td>
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<tr>
<td>Latency S-amplitude, mc</td>
<td>2.68±1.00</td>
<td>2.97±1.57</td>
<td>-0.286</td>
<td>0.421</td>
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<tr>
<td>NCV, n. sural, m/s</td>
<td>23.32±12.70</td>
<td>24.32±14.45</td>
<td>-0.437</td>
<td>0.208</td>
</tr>
</tbody>
</table>

The 1st group was characterized by the highest serum level of BDNF (4.38±1.55ng/ml) versus patients of 2nd group (2.35±1.24ng/ml, p=0.002). The highest level of TrkB was detected in the 2nd group (5.12±1.56ng/ml), versus the average levels of the 1st group (3.21±1.55ng/ml, p=0.001). The inverse dependence between serum TrkB and severity of pain by Pain Detect (R=−0.572, p=0.005) were revealed.

Conclusions:: Low serum level of TrkB testifies to relatively intact transmembrane receptor, which can
bind with an excess of BDNF and implements its hyperalgesic intracellular effects. On the contrary, severe DPN is associated with a high serum amount of non-functional TrkB, which can lead to painless form polyneuropathy.
TOPOGRAPHICAL AND DIPOLAR ANALYSIS OF LASER EVOKED POTENTIALS IN FIBROMYALGIC PATIENTS WITH NON LENGHT DEPENDENT SMALL FIBER NEUROPATHY

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Background and Aims:: Research on Fibromyalgia (FM) is currently based on interesting pathogenetic hypothesis based on the involvement of the central and peripheral nervous system. Recent studies have shown an altered central processing of nociceptive inputs as well as a small fibers neuropathy (SFN) in a large number of fibromyalgic patients. Objectives: 1) to evaluate Laser Evoked Potentials (LEPs) in FM patients, taking into consideration skin innervation and comparison with control group 2) to identify cortical sources of LEPs in consideration of skin biopsy results.

Methods:: We evaluated 57 fibromyalgic patients already included in Vecchio et al. (2020) and 15 healthy age and sex matched controls. All patients were examined with multichannel LEPs and with skin biopsy as described respectively in de Tommaso et al. (2014) and in Vecchio et al. (2020). sLORETA software was used to localize generators of LEPs.

Results:: Skin biopsy showed in 22 patients proximal denervation (FMP), in 18 patients normal skin innervation (FMN) and in 7 patients SFN in proximal and distal crural sites (FMD). The sLORETA analysis highlighted a reduced activation of Brodmann area 32 in FMP and area 33 in FMD compared to controls after knee stimulation and a reduced activation of the dorsolateral cortex in the FMP and FMN groups in comparison to controls after foot stimulation.

Conclusions:: Denervation can cause a deactivation of the cingulate and the dorsal-latero-frontal area, which can determine altered pain modulation.
DIFFUSE NOXIOUS INHIBITORY CONTROL MODULATES THE N13 SPINAL COMPONENT OF SOMATOSENSORY EVOKED POTENTIALS

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Background and Aims:: The dorsal horn generator of the N13 component of somatosensory evoked potentials (SEPs) is not clearly understood. To verify whether wide-dynamic-range (WDR) spinal neurons in the dorsal horn are involved in the generation of the N13 SEPs; we tested the effect of diffuse noxious inhibitory control (DNIC), a modulator of WDR neurons, on N13 SEPs in healthy humans.

Methods:: Twelve healthy subjects (age 26.7±4 years, 5 males) were enrolled. The cold pressor test on the left foot was used as a heterotopic noxious conditioning stimulus to trigger DNIC. We tested the pressure pain threshold at the thenar muscles of the right hand to verify the effectiveness of our DNIC paradigm. We then recorded SEPs after right median nerve stimulation before, during, and after the cold pressor test.

Results:: The cold pressor test increased pressure pain threshold by 15% (p=0.04). The amplitude of the N13 SEPs component during the cold pressor test was significantly lower than that recorded at baseline (by 25%, p=0.04).

Conclusions:: We showed that a heterotopic noxious conditioning stimulus significantly reduced N13 SEPs amplitude, suggesting that the generators of this spinal SEPs component are sensitive to DNIC. This finding suggests that the N13 SEPs is generated by the segmental postsynaptic response of dorsal horn WDR neurons and support the use of N13 in the assessment of dorsal horn excitability during central sensitization.
Background and Aims:: Back pain is very common in the general population, but even more so among people with multiple sclerosis (MS), with a prevalence of up to 50%. But it is difficult to associate back pain with MS in most cases. These syndromes can have different nature and mechanisms of pain and sometimes their combination.

Methods:: 120 patients with MS were examined and their history was analyzed at the Lviv regional multiple sclerosis center. Standardized questionnaires VAS, PainDetect, HADS, SF-36 were used to assess the characteristics of pain, anxiety, depression, and quality of life in these patients.

Results:: During the last month, 28 patients (23,3%) had back pain associated with MS. 10(8,33%) patients had Lhermitte’s sign (LS), 4(3,33%) had back pain associated with postural abnormalities (PABP), 14(11,66%) patients had other back pain (OBP). 60% of patients with LS and 64,29% with OBP considered these pain syndromes as the most disturbing in the structure of MS. 90% of MS patients with LS were female and they had high rates of pain intensity and were characterized by the presence of a neuropathic component of pain and high levels of anxiety. For patients with PABP and OBP prevalence of the nociceptive component of pain was more typical. PABP occurs among patients with a longer duration of MS and they have lower levels of the physical component of quality of life.

Conclusions:: Understanding the structure and characteristics of back pain syndromes and their association with MS will improve the diagnosis and treatment of these patients.
SOUND-INDUCED FLASH ILLUSIONS SUPPORT CORTEX HYPEREXCITABILITY IN FIBROMYALGIA

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Background and Aims:: Sound-induced flash illusions (SIFI) reflect visual cortical excitability. In this case-control study, we explored whether SIFI are perceived differently in patients affected by fibromyalgia, in healthy controls and in patients with fibromyalgia and migraine together.

Methods:: Forty-one patients affected by fibromyalgia (mean age 49.8±10.65 years; 38 females) and in forty-one healthy controls (mean age 47.26±4.9 years; 34 females) were enrolled and matched for gender and age. A single flash with multiple beeps was given to induce fission illusion (1F0B, 1F1B, 1F2B, 1F3B, 1F4B), whereas multiple flashes with a single beep were induced fusion illusion (2F0B, 2F1B, 3F0B, 3F1B, 4F0B, 4F1B). Finally, we compared the number of perceived flash in fission and fusion illusion using multivariate analysis of variance between groups.

Results::

Patients affected by fibromyalgia perceived fewer flashes than controls with reduction of fission illusion when a single flash was combined with multiple beeps (F₁F₁B=5.74, p=0.019, F₁F₂B=22.79, p<0.001; F₁F₃B=22.45, p<0.001; F₁F₄B=11.23, p=0.001). On multiple flash trials, fusion illusion was less consistently reported in both groups, but not completely disrupted for some trial conditions (F₃F₀B=4.254 p=0.043; F₄F₀B=4.39 p=0.04). Finally, the group fibromyalgia plus migraine reported fewer flashes than healthy controls and patients with only fibromyalgia in some experimental conditions (e.g., 1F₂B, 1F₃B, 1F₄B), without statistical significance (all p>0.05).

Conclusions:: The reduced illusory fission effects in fibromyalgia might indicate an increased cortical...
responsivity supporting the potential role of cortical hyperexcitability in fibromyalgia. Cross-modal illusions represent a valid tool for exploration of cross-sensory functional connectivity, which likely has an important role in the pathophysiology of fibromyalgia.
THERAPEUTIC EFFECT OF ONABOTULINUMTOXINA (BONT/A) IN PIRIFORMIS SYNDROME RESISTANT TO CONVENTIONAL THERAPY

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Background and Aims:: Objective: To describe the therapeutic effect of OnabotulinumtoxinA in a case of piriformis syndrome. Background: Piriformis syndrome is due to entrapment of the sciatic nerve by the piriformis muscle, in the absence of a lumbar radiculopathy.

Methods:: We conducted open administration of 3 cycles of 50 units of OnabotulinumtoxinA (BoNT/A) injections in the piriformis muscle every 9 months in a patient with Piriformis Syndrome. Analgesic medication used by the patient was recorded periodically before and after of BoNT/A injections as well as patient subjective rating and Visual Analog Scale (VAS).

Results:: A 38-year-old man with 6 years of continuous pain in right buttock, pelvic pain and right leg that increased when attempting to walk (VAS: 9), causing a significant interference in activities of daily living. No improvement with analgesics, muscle relaxants and neuromodulators. After of each OnabotulinumtoxinA injection the patient had a significant subjective improvement in pain of 90% (VAS: 4) and his activities of daily living for 9 months, without side effects, and achieved a 92% of reduction in the use of medication compared to baseline.

Conclusions:: OnabotulinumtoxinA was effective to control pain in our patient with refractory piriformis syndrome, improving his quality of life.
CAN THE SONOGRAPHIC DISTAL VASTUS MEDIALIS THICKNESS BE A USEFUL MARKER TO REFLECT DISEASE PROGRESSION OF KNEE OA?

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Background and Aims:: The objective of this study was to evaluate the correlations between radiologic staging and evaluated ultrasound results of the distal portion of VM muscle thickness in knee OA comparing with the previous mid-thigh level study.

Methods:: Knee OA was graded according to the Kellgren-Lawrence classification. We measured the femur length using the distance from the surface landmark of ASIS to the lateral border of the patella. Then the mid-level (50%), and distal 25% of the femur level were calculated. At the mid-level, thickness of the rectus femoris, vastus intermedius, and VM was measured, and at the distal 25% level, VM muscle thickness was measured (Fig 1).

Results:: We included 30 patients (20 women and 10 men) aged 20 to 80 years. The subgroup was divided into two groups according to the severity of knee OA (Group 1: K-L grade 0-1, Group 2: K-L grade 2-4). A significant negative correlation between the thickness of some anterior thigh muscle and stage of knee OA was noticed. When the body mass effect was considered, it showed a more significant result between groups 1 and 2 (Table 1). With subgroup analysis, a statistically significant difference was determined in every muscle we investigated (Table 2).

Conclusions:: Individual thigh muscle thickness showed a negative correlation with the progression of knee OA. With the easy accessibility and high reproducibility, exploring the thickness of the distal portion of VM can be a useful indicator for severe knee OA patients.
Background and Aims:: Pain is a highly disabling non-motor symptom of Parkinson’s disease (PD). In advanced PD stage, pain frequently occurs or is aggravated in the “off” state and ameliorates by increasing dopamine replacement therapy (DRT). Levodopa/carbidopa intestinal gel (LCIG) is useful in advanced PD patients with severe complications. LCIG may help optimizing the risk/benefit ratio of DRT and ameliorate quality of life (QoL) in advanced PD patients.

Methods:: Study of the clinical course of a PD patient candidate for LCIG and with painful dystonia.

Results:: A 77-year-old female was diagnosed with PD in 2004 and initiated DRT in 2005. In the last 2 years, she kept suffering from painful peak-dose dystonia, followed by severe “off” state; moreover, she was in “off” state for most night-time. She was proposed switching to LCIG. Along the 3-day test tube phase with 24-h infusion, dystonia almost disappeared, and the patient reported marked reduction of pain severity. After PEG-J positioning, the patient was discharged under 24-h infusion treatment. At 2-month follow-up visit, the patient was able to walk with assistance, night-time sleep was significantly improved and pain severity was greatly reduced. She reported moderate limb dystonia, occurring soon after tube cleansing.

Conclusions:: Non-motor symptoms may benefit from switch to LCIG. Here we show the benefit of switch to LCIG in a PD patient suffering from severe peak-dose levodopa-related dystonia. These findings strengthen the need for optimizing DRT with the aim of managing motor and non-motor symptoms to reduce disability and ameliorate QoL and autonomy.
CLINICAL SIGNS OF OPIOID OVERDOSE IN A PATIENT ON GABAPENTIN AND OXYCODONE

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Background and Aims:: The pain control in some chronic or acute conditions can be a difficult problem. A few levels model is often used for post-surgical patients. Oxycodone and gabapentin are used in many patients together. This combination may have some harmful potential in some circumstances.

Methods:: The patient had physical examination, imaging, blood tests.

Results:: We present a case of a patient who after 10 mg Oxycodone MR and twice given 300 mg gabapentin suffered worsening with a clinical picture of opioid overdose; the condition was successfully influenced with 400 mcg Naloxone. The patient had no significant problems further.

Conclusions:: The probable risk of combining gabapentin and oxycodone has already been described, but the mechanism remains still unclear.
LONG-TERM PAIN FREE EFFECT OF PLATELET-RICH PLASMA INJECTION IN A HIGHLY FREQUENT CASE OF SACROILIAC JOINT PAIN

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Background and Aims:: Background Sacroiliac joint pain (SIJP) is one of the most common debilitating disorders that can affect an otherwise healthy productive person. This can be due to combination of inflexible sacroiliac joint structure and disregardable risk factors such as bad posture and prolonged immobility. Platelet-rich plasma (PRP) injection is one of the most recent, promising and less explored modalities, particularly in Indonesia. Aims To report a case of highly frequent relapse of SIJP.

Methods:: Case A 46-year-old, obese male with no other known risk factors other than prolonged position due to his occupation as a commercial pilot. He suffered from frequently relapsed (less than 6 months interval) intense radiating back pain down to left posterior thigh with pain score of 8/10 and 34% of Oswestry Disability Index (ODI). He had no prior history of trauma nor related back surgery. Physical examination revealed the pain was localized to the left posterior superior iliac spine (PSIS) with positive Faber and straight leg raising test. Lumbar imaging yielded mild disc degeneration of L5-S1 and spondyloarthrosis. He was previously treated with conservative (oral medication, physiotherapy) and interventional (corticosteroid injection) therapy. Single PRP intra-articular injection was done under C-arm guidance (Fig. 1).
Results: Despite no change in his modifiable risk factors, he is pain free for 3 years with 0/10 in numeral pain score and 2% of ODI in follow up.

Conclusions: Conclusion PRP is one of modalities in treating SIJP that can be considered in a highly frequent relapse case.
LONG-TERM EFFICACY OF SINGLE BOTULINUM TOXIN-A INJECTION IN A RELAPSING PIRIFORMIS SYNDROME CASE

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Background and Aims:: Background Piriformis syndrome (PS) has been considered as a complex diagnosis thus often making its management become complicated. Management of PS ranges from conservative therapies to interventional including injection and surgeries. Among interventional methods, local anesthetic and steroid injections are more commonly practiced. However, due to its negative effect, serial botulinum toxin-A (BTX-A) injections has been proposed as an alternative therapy that can provide relief. Aims To report a long term relief of pain in case of persistent PS with single BTX-A injection.

Methods:: Case An otherwise healthy 41-year-old female weekly basis relapse of classic PS. She complained sharp radiating gluteal pain with no neurological deficits. Diagnosis of PS was confirmed from positive trigger point, provocative test (FAIR, Beatty and Pace maneuver) and diagnostic block. She was initially treated with combination of local anesthetic and corticosteroid injections but failed to provide long-term relief with relapsing 8/10 score of pain. Considering the negative effects from multiple local anesthetic and steroid injections, an alternative method of 100 IU BTX-A intra-muscular injection was done (fig. 1).
**Results:** Result She reported improvement in pain score from 8 to 3 in 15 minutes post injection, with further decrease in pain score to 0 after two weeks and no complications. Thus no additional injection was performed. She is now pain free for 1.5 years with no report of additional relapses.

**Conclusions:** Conclusion BTX-A injection can be considered as an alternative to provide a long term relief in a frequent relapse case of PS.
THE IMPACT OF SMALL FIBER DAMAGE ON SOMATOSENSORY DISTURBANCES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A CLINICAL, NEUROPHYSIOLOGICAL AND SKIN BIOPSY STUDY.

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Background and Aims:: Peripheral neuropathy is one of the most common neurological manifestations of SLE. Though patients with SLE often complain about painful somatosensory disturbances, the prevalence and clinical impact of nociceptive small fibers damage have been poorly studied in this condition. Our prospective study aims at assessing how small fibers damage impacts on painful symptoms and at disclosing clinical and diagnostic variables associated to small fibers impairment in patients with SLE.

Methods:: We consecutively enrolled 22 patients suffering from SLE with painful disturbances. Each patient underwent clinical examination, DN4, SFN-SIQ, NPSI, Pain Catastrophizing questionnaires, nerve conduction study, quantitative sensory testing (QST) and skin biopsy. Small fiber neuropathy was diagnosed by distal skin biopsy intraepidermal nerve fibers density (IENFD) reduction associated to at least one thermal detection threshold abnormality at QST.

Results:: 32% patients showed a pure small-fiber neuropathy, 10% a mixed neuropathy with both large and small fibers involvement. 75% showed both proximal and distal IENFD reduction at skin biopsy. Small fiber damage presence and IENFD reduction were associated to higher DN4 scores, pain hypoesthesia and higher QST mechanical pain threshold (MPT) at foot.

Conclusions:: Small fiber damage with a non-length dependent distribution is a common finding in patients with SLE and is significantly associated to pain of neuropathic quality as assessed by DN4 questionnaire. DN4 for distal pain, besides clinical and QST evaluation of the foot pain sensitivity, could be valuable diagnostic tools to screen for small fiber neuropathy in patients suffering from SLE.
EVALUATION OF DULOXETINE EFFECTIVENESS IN PAIN RELIEF FOR PARKINSON'S DISEASE PATIENTS

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Background and Aims: To study effectiveness of duloxetine for relief of pain in Parkinson's disease.

Methods: A double-blind, placebo-controlled study was conducted for 3 months. Patients with Parkinson's disease were selected according to the following criteria: with chronic pain in stage I-III of Hoehn & Yahr scale. From this group of samples in a random order, patients were divided into placebo groups and duloxetine groups. In the second group, patients received 30 mg of duloxetine once a day with a gradual increase in dose up to 60 mg. Results were evaluated using of 11-point Visual Analogue Scale and Short-Form McGill Pain Questionnaire, as well as a miniature pain stimulus were used to determine the subjective threshold of pain sensitivity. Threshold of pain sensitivity for each of the subjects was established after the application of the "multiple random stairs" method.

Results: At the beginning of study, there was no statistically significant difference in demographic and clinical data between duloxetine group and placebo group. Quantitative improvements were observed in evaluations of the 11-point Visual Analogue Scale and Short-Form McGill Pain Questionnaire in favor of duloxetine group (p = 0.04). In the induced pain stimulus was noticeable increase in pain thresholds in the duloxetine group compared with the placebo group (p = 0.05).

Conclusions: The efficacy of duloxetine in pain relief was determined in patients with Parkinson's disease, further studies are needed to understand the effectiveness of duloxetine with prolonged use.
NEUROPHYSIOLOGICAL AND CLINICAL EFFECTS OF TSDCS IN PATIENT WITH CHRONIC PAIN

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Background and Aims:: Chronic pain (CP) is complex clinical condition, often devastating for patients and unmanageable with pharmacological treatments. Several findings indicate that transcutaneous spinal direct current stimulation (tDCS) might represent a complementary therapy in managing CP. In this randomized, double-blind, sham-controlled crossover study, we assess tDCS effects in CP patients.

Methods:: Sixteen patients (aged 65.06 ± 16.16 years, 8 women) with CP of different etiology underwent sham and anodal tDCS (anode over the tenth thoracic vertebra, cathode over the somatosensory cortical area - 2.5 mA, 20 min, five days for one week). As outcomes, we considered the Visual Analogue Scale (VAS), the Neuropathic Pain Symptom Inventory (NPSI), and the components of the lower limb flexion reflex (LLFR), i.e., RIII threshold, RII latency and area, RIII latency and area, FR total area. Assessments were conducted before (T0) and at the end of the treatment (T1), and after one week (T2) and one month (T3).

Results:: Compared to sham, anodal tDCS reduced RIII area at T2 by more than 50% (p=0.0043) and T3 by about 50% (p=0.0012); similarly, FR total area was reduced at T3 by about 50% (p=0.03). Clinically, anodal tDCS dampened VAS score at T3 by about 50% (p=0.015), and NPSI score at T1 (p=0.0012) and T3 (p=0.0015) by about 30%, compared to sham. Changes in VAS and NPSI scores linearly correlated with the reduction in LLFR areas (p=0.0004).

Conclusions:: Our findings suggest that anodal tDCS could modulate central nociceptive signal transmission and pain perception in CP conditions.
QUALITY OF LIFE AND PAIN IN PARKINSON DISEASE: A PROSPECTIVE STUDY

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**Background and Aims::** Introduction: Pain is a common non-motor symptom in Parkinson disease (PD), which can be disabling. The objective of this work is to describe the epidemiological aspects of pain in PD and its impact on the patient’s quality of life.

**Methods::** This is a prospective analytic study conducted in the neurology department of Mohamed VI hospital university in 80 patients suffering from PD. Demographics, clinical features and medication data were obtained using a structured questionnaire and the clinical classification of Ford.

**Results::** the analysis showed that the mean age was 62.92 (range from 42 to 90), pain was prevalent in 65% of PD patients, men were more affected than women (males 59.57%), five different types of pain were reported: musculoskeletal pain (42.5%), nerve/nerve root pain (38.8%), primary/central pain (16.3%), dystonic pain (12.5%) and akathisia (12.5). Fifty nine percent of the patients reported the pain on the off period, (1.92%) on the on period and (38.46) on both periods. There was no difference statistically significative in the distribution of depression depending on the presence or absence of pain. The quality of life was impacted with the presence of a musculoskeletal pain.

**Conclusions::** Conclusion: pain is a common non-motor symptom in Parkinson disease, but it is probably infradiagnosed. For a correct treatment, it must be well identified and clinically classified.
CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY: FROM SYMPTOMATOLOGY USING QUANTITATIVE SENSORY TESTING TOWARDS EFFECTIVE TREATMENT

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Background and Aims:: Chemotherapy-induced peripheral neuropathy (CIPN) affects up to 80% of patients after treatment with e.g. paclitaxel or oxaliplatin. Preclinical research elicits sensitization of temperature- and mechanosensitive Transient Receptor Potential (TRP) channels as potential mechanism behind this debilitating pathology. The current study evaluates TRP involvement in human by assessing thermal and mechanical sensitivity in patients with CIPN.

Methods:: Quantitative Sensory Testing is performed bilaterally on the proximal phalanx of the index finger in patients previously treated with paclitaxel or oxaliplatin, and age-matched healthy controls. Von Frey hairs are used with an ascending-descending principle to determine the mechanical detection and pain thresholds. Heat and cold detection and pain thresholds are assessed with a thermal cutaneous stimulator using the method of limits, ranging from 0°C to 60°C.

Results:: Sixteen subjects have been included so far. Therefore, no statistical analysis has yet been performed. However, a trend towards higher heat detection thresholds (mean±SEM) can already be distinguished for paclitaxel and oxaliplatin versus healthy controls (41.6±1.9°C and 42.3±0.9°C vs. 37.0±0.7°C, respectively, Figure 1A). Also, paclitaxel reduces the mechanical pain threshold (mean±SEM) compared to healthy controls (84.1±41.7g vs. 168±28.9g, respectively, Figure 1B). By October 2021, approximately 60 subjects will have been included.

Conclusions:: Preliminary data suggest that paclitaxel and oxaliplatin induce heat hyposensitivity. Alterations in thermal or mechanical sensitivity may provide evidence for the involvement of temperature- or mechanosensitive TRP channels in CIPN in human. In the near future, linkage of such altered sensitivity to direct TRP functionality assessments will further support novel TRP-based medicines for CIPN.
HIGH BETA EEG FUNCTIONAL CONNECTIVITY IS DECREASED IN THE LEFT AMYGDALA OF FIBROMYALGIA PATIENTS IN CORRELATION WITH THE AFFECTIVE COMPONENT OF PAIN.

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Background and Aims:: Fibromyalgia is a major chronic disease associating mainly pain, prominent affective dysfunction, sleep disorders and fatigue. Changes in neurotransmitters activity and in brain connectivity have been associated to pain in fibromyalgia, however, electrophysiological data on correlates of the affective dimension of pain lack.

Methods:: In this data analysis from a wider case-control study, we explored resting-state EEG connectivity (spectral analysis and coherence) in the beta domain (supposedly indexing the GABAergic neurotransmission highly involved in pain regulation), in 16 fibromyalgia patients and 11 age-matched healthy controls. In addition, we recorded affective and sensory pain components (patients), as well as mood and sleep descriptors (patients and controls).

Results:: A decrease in functional connectivity was noticed in the high beta (20-30 Hz) sub-band of patients (p=0.039) in the left laterobasal complex of the amygdala, correlated with the affective component of pain (r=0.50, p=0.049). An increase observed in the low beta (13-20 Hz) relative power in the left DLPFC and in the VLPFC of fibromyalgia patients (respectively p=0.001 and 0.033) was correlated with the ongoing pain intensity (r=0.54 and 0.71, p=0.032 and 0.002).

Conclusions:: For the first time, we showed a decreased connectivity related to the GABAergic system in the amygdala, associated with the affective component of pain (expected in this structure highly involved in the affective regulation of pain). The increased beta power in the prefrontal cortex could be compensatory of the overall GABAergic dysfunction in chronic pain.
MERALGIA PARESTHETICA ASSOCIATED WITH WEIGHT LOSS

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**Background and Aims:** Belts and tight-fitting clothing, obesity, and pregnancy are all common causes of compression of the Lateral Femoral Cutaneous Nerve (LFCN) also known as Meralgia Paresthetica (MP). But the LFCN can be vulnerable to other sources of traction as it passes beneath the inguinal ligament. We sought to consider if MP, much to our surprise, could be caused by weight loss.

**Methods:** A review of the literature and commonly used references such as UpToDate was completed to search for the possibility that mechanical factors involved with loss of weight might contribute to Meralgia Paresthetica. This effort was undertaken when a 63 year old non-Diabetic man presented to our clinic with the classic features of LFCN syndrome without any of the commonly associated risk factors and rather than weight gain, he had lost 30 pounds during the recent pandemic.

**Results:** The most commonly identified risk factors for MP are obesity, diabetes mellitus, and older age, pregnancy, increased abdominal girth such as in ascites. Mechanical traction on the nerve due to prolonged leaning against a table or bench, carrying heavy objects supported by the groin, various exercises have also been associated. Postoperative MP is also cited as cause of the compressive neuropathy. But weight loss is not described.

**Conclusions:** Meralgia Paresthetica is a mononeuropathy of the LFCN and like other neuropathies, injury can be due to various causes with the ultimate result being local ischemia. We report on a case of such injury occurring due to mechanical effects from weight loss rather than weight gain, obesity, or other causes usually cited.
REFLEXOTHERAPY AND CHRONIC LOWER BACK PAIN

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Background and Aims:: Lower back pain (LBP) affects 90% of the population. Objective: to study the effect of acupuncture on the relief of exacerbations of chronic LBP.

Methods:: 100 patients with chronic LBP were divided into two groups. The main group - 50 patients (48.55 ± 14.4). Patients underwent reflexology daily for 10 days along with standard drug therapy. The control group consisted of 50 patients (47.92 ± 14.0) with standard drug therapy. Pain intensity was evaluated with numeric rating scale for pain, kinesiophobia on the Tampa Scale for Kinesiophobia, anxiety and depression on the hospital anxiety and depression scale.

Results:: pain intensity decreased by 57% from 6.61 ± 0.54 to 2.92 ± 0.31 points in the main group, by 14% from 5.72 ± 0.84 to 3.12 ± 0.50 points in the control group after 10 days of therapy. Kinesiophobia decreased by 11% in the main group and by 9% in the control group. The level of anxiety decreased from 8.66 ± 1.04 to 7.06 ± 1.32 points and from 9.24 ± 1.13 to 7.14 ± 0.82 points, the level of depression from 7.22 ± 0.88 to 6.18 ± 1.11 points and from 6.58 ± 0.79 to 5.84 ± 0.93 points respectively in the main and control groups after 10 days.

Conclusions:: Reflexotherapy is an effective method of short-term relief of exacerbation in patients with chronic LBP, but does not significantly affect the degree of kinesiophobia and manifestations of anxiety and depression.
CANCER-RELATED NEUROPATHIC PAIN (CRNP) IN EUROPE: WHAT ARE THE GAPS IN DIAGNOSIS AND TREATMENT FROM PATIENTS' PERSPECTIVE?

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Background and Aims:: Cancer burden on individuals and society is high with 2.7 million new cancer cases per year in Europe. With effective treatments available, people with cancer live longer but often with sequelae such as neuropathic pain resulting from the cancer or its treatment. People with cancer experiencing neuropathic pain from 13 European countries shared their experiences with the diagnosis and management of their pain.

Methods:: An online survey, prepared, conducted and analysed with a team of experts including physicians, nurses and patients, was completed in June 2021. Adults consenting to participate and diagnosed with cancer were screened for symptoms of neuropathic pain. Respondents who met three or more of the DN4 (Douleur Neuropathique 4) criteria were enrolled and provided detailed information about their experiences relating to the diagnosis and management of CRNP.

Results:: Out of 24,733 screened respondents, 549 persons living with CRNP were recruited. Of those recruited, 88% were ≤ 65 years old, 32% experienced severe pain daily and 89% fulfilled ≥4 DN4 criteria. CRNP locations included arms/hands/fingers (63%), legs/feet/toes (60%), torso/chest/body/back (62%), and at surgical site (29%). Although CRNP symptoms were present, 40% had not received a formal diagnosis of neuropathic pain. Those with CRNP diagnosis were more likely to get pharmaceutical treatment (67% vs 44%) or physiotherapy (35% vs 22%) and were more likely to be satisfied with their treatment (67% vs 43%).

Conclusions:: Diagnosis of cancer-related neuropathic pain remains a challenge and many of those affected seem to remain unrecognised. Those without diagnosis are less likely to be treated for pain.
COMPARISON OF PATIENTS WITH L5-S1 INTRAVERTEBRAL DISK HERNIATION THAT EXPERIENCED ACUTE AND CHRONIC PAIN

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Background and Aims:: Discogenic lower back pain remains a common and challenging problem to solve. The intervertebral disk can be a source of acute or chronic pain. It is still not clear what causes some people to suffer more than others, but there appear to be links to mechanisms of psychological and biological sensitization. This can be due to individual response to stress. Cortisol is frequently been associated with various stress related disorder.

Methods:: A total of 60 patients with L5-S1 intravertebral disk herniation were recruited. MRI of lower back was performed for all participants. The first group (30) included patients who experienced acute pain, and the second group (30) with pain that last more than 3 months. Both groups were assessed with morning serum cortisol level and DN4 questionnaire before the treatment.

Results:: The group with chronic pain showed significantly higher (p<0.05) level of morning serum cortisol level (1.34±0.25 mg/l) than acute pain group (0.51±0.32 mg/l). According to DN4 questionnaire we found that neuropathic type of pain is found in patients with acute pain (93%) statistically more often (p<0.05) than with chronic pain type (53%).

Conclusions:: In contrast to acute pain, people suffering from chronic pain report amplified rather than decreased pain over time. Recent theories have suggested that chronic pain could be partly maintained by the endocrine stress response. Results showed that patients with chronic back pain have higher levels of serum cortisol, which can possibly affect healing and prolong recovery time.
EFFECT OF BALANCE TRAINING WITH BOSU BALL ON SUBJECTS WITH CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY

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**Background and Aims::** Among patients undergoing chemotherapeutic regimens for cancer treatment chemotherapy-induced peripheral neuropathy (CIPN) is a common adverse effect, wherein patients experience symptoms like decreased proprioception, decreased sensation, reduced balance and weakness in lower extremities leading to increased risk of falls. The present study aimed to evaluate the effect of balance training with BOSU ball on balance in subjects with CIPN.

**Methods::** A total of 27 subjects (21 females, 06 males) with a modified total neuropathy score (m-TNS) score of >5 were included in the study. Pre and post-assessment scores were noted using the Berg balance scale (BBS), functional reach test (FRT) and one leg standing test (OLS).

**Results::** Paired ‘t’ test was used to analyze the important pre and post-scores BBS, FRT, OLS with p≤0.05 with physiotherapy intervention of 01-week significant improvements in BBS, FRT and OLS were noted (p <0.01).

**Conclusions::** Balance training with BOSU ball and exercises was demonstrated improvements in balance. However, similar study may be carried out in larger sample size to substantiate the evidence.
BOTULINUM TOXIN IN PAIN TREATMENT: ABOUT 100 PATIENTS

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Background and Aims:: Considered once the most toxic substance in the world, botulinum toxin (BTX) is presently under a more engaging day. Its medical use has gained an important extension that still support the validation of some clinical trials, this is the case of pain.

Methods:: We report a clinical experience with 100 patients who presented chronic pain phenomenon, such as migraine, tension headache, lower back pain, painful diabetic neuropathy, post herpetic neuralgia and trigeminal neuralgia. All patients presented a pain\(\geq 7/10\) on the visual numeric scale (VNS), with or without prior treatment. They were treated with BTX type A each 3 months and followed for 12 months. The doses and routes used were: Migraine (30u, 12 sites/4muscle groups); tension headache (30u, 6sites/2muscle groups); LBP (20u, 8 sites/2muscle groups); PHN and TN (0, 5-1u/cm2 intradermally) and PDN (1-2 u/cm2 subcutaneous).

Results:: The sex ratio (F/M) was 1.3 and the average age was 43.3 years with age limits of 11 and 79 years. It was noted 26% of TN, 23% PDN, 20% migraine, 15% LBP, 11% headache and 5% PHN. The average gain (decrease) on VNS was 4.11 points. The gain was 5.6 points for TN, 5.3 for PHN, 5 for LBP, 4.2 for tension headache and 3.2 for PDN. Migraine attacks decreased from 4.1 to 1.2 per month with a gain of 1.4 points on VNS.

Conclusions:: It is evident that BTX has an analgesic effect which has been demonstrated with several clinical studies. Future research should include expanding domains of treatable diseases, doses, injection intervals and complications.
CLINICAL CHARACTERISTICS OF LOW BACK PAIN IN PATIENTS WITH HYPERMOBILITY SPECTRUM DISEASES

Dina Khaibullina, Yuri Maksimov, Elvira Ihsanova, Dmitriy Busygin, Elza Rakhmatullina, Olga Kochergina, Lidia Kadirova, Oksana Alekseeva, Rady Esin

Background and Aims:: The diseases of the hypermobility spectrum (DHS) influence the clinical characteristics of Low Back Pain (LBP). The purpose of the study: to identify the clinical features of LBP in patients with DHS.

Methods:: 250 people were examined (147 men and 103 women) with LBP aged 18 to 45 years. External signs of the DHS were detected in 95 (38.0%) people. The control group amounted to 30 patients with LBP without DHS.

Results:: The degree of joints hypermobility in 4 points was revealed in 22.1%, 5-6 points - in 50.5%, 7-8 points - in 16.8% and 9 points - in 10.6% of cases. The character of pain was described as "pulling" in 30 (31.6%), "biting" at 27 (28.4%), "rodent" at 15 (15.8%), "scoring" at 23 (24.2 %) cases. The pain intensity was characterized by patients with DHS as "moderate" - 69.4%, "tolerant" - 30.5%, "unbearable" - 0.08%, in the control group 76.6%, 20% and 3.4%, respectively. The pain severity in the visual analog scale in patients with DHS was 6 +/- 1.3 points, in the control group 5 +/- 0.6 points. In case of LBP on the background of the DHS, static functional deformations of the spine, the functional blockade of sacroiliac joints and vertebral segments were also more common (p≤0.05) compared to the control group.

Conclusions:: Patients with LBP on the background of the DHS have a larger spectrum and the degree of clinical manifestations compared to patients without DHS.

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Background and Aims:: Patients who have undergone Covid-19 with maxillofacial complications suffer from headaches and local pain for a long time. Purpose: monitoring the clinical course of the nature of pain syndrome in the maxillofacial region of patients with Covid-19.

Methods:: Clinical analysis was carried out on 78 patients who applied to the TMA clinic. The average age of patients was 60 ± 9.0 years, including 41 women (54%) and 37 men (46%), with the diagnosis of cavernous sinus thrombosis, maxillar osteomyelitis 1–3 months after the onset of acute Covid-19 disease. During 1 years of rehabilitation, the pain was assessed according to a 10-point criterion (pain load - 0 points, very strong - 10 points) through the questionnaire.

Results:: In addition to inflammation in these patients, include headache, dizziness, n. Facialis paresis in 39 patients, paresthesia of the 3rd corneal nerve in all patients. In the beginning, severe irradiating headaches were observed in 85% of cases, and in some patients, in the absence of taking non-steroidal anti-inflammatory drugs, the need for narcotic analgesics, sedatives, tranquillizers. During observation, severe pain was in 40% of patients (8-10 points), and in 25% of patients, the average simultaneous pain remained within 3.5 ± 0.18 (p≥0.05). In 15% of patients, the headache persisted up to 4-5 (on average) points. The mean pain score was 3.6 ± 0.13 (p ≥ 0.05) in all patients end of the year.

Conclusions:: In patients undergoing COVID 19, thrombosis, facial bone necrosis was very long-term, predominant headaches. In 40% of patients, severe pain persisted for years.
CAUDAL EPIDURAL PULSED RADIOFREQUENCY FOR DISTAL SYMMETRICAL POLYNEUROPATHY

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Background and Aims:: Background distal symmetrical polyneuropathy (DSP) present with numbness, tingling, pain, and/or weakness starting in the toes and progressing proximally in a stocking-glove distribution. Still there are no specific treatment Objective: in this study, clinicians use caudal epidural pulsed radiofrequency (CPRF) for the management patients complain from sensory symptom of DSP.

Methods:: CPRF stimulation for twenty four patients with DSP had sensory symptom not response to treatments. Inserted a caudal cannula into the epidural space through the sacral hiatus under fluoroscopy or ultrasound guidance. After Sensory and motor PRF, administered PRF at 5 Hz with a 5-ms pulse width for 600 seconds at 45 V. The effect of stimulation was evaluated using a numeric rating scale (NRS) within first week and monthly for 3 months after the procedure. Successful pain relief was defined as a reduction in the NRS score of ≥ 50% as compared with the score prior to treatment. In addition, at 4 months after treatment, patient satisfaction levels were examined; patients that reported “very good” (score = 7) or “good” (score = 6) results were considered to be satisfied with the procedure.

Results:: Neuropathic pain was significantly reduced in four visit after PRF (P < 0.001, repeated measures one-factor analysis). In addition, at 3 months post-PRF, more than half of the patients achieved a successful response (≥ 60% pain reduction) and were satisfied with treatment results.

Limitations:: limited number of patients and short duration of the study.

Conclusions:: CPRF safer, cheaper and more relieve of symptoms.
ULTRASOUNIC APPROACH CAUDAL EPIDURAL PULSED RADIOFREQUENCY

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Background and Aims:: Background: The recently introduced pulsed radiofrequency (PRF) technique is used to provide relief from neuropathic pain had done under C-arm fluoroscopy. Objective: In this study use ultrasounic guided for caudal epidural pulsed radiofrequency (CPRF) for the management of neuropathic pain and central sensitivity syndromes.

Methods:: a prospective study CPRF stimulation for thirty patients with neuropathic pain or central sensitivity syndromes. Linear prope ultrasound (Sonosite) guidance for inserted a 22-gauge cannula into the epidural space through the sacral hiatus. After Sensory and motor PRF, administered PRF at 5 Hz with a 5-ms pulse width for 600 seconds at 45 V. The effect of stimulation was evaluated using a numeric rating scale (NRS) within first week and monthly for 3 months after the procedure. Successful pain relief was defined as a reduction in the NRS score of ≥ 50% as compared with the score prior to treatment. In addition, at 4 months after treatment, patient satisfaction levels were examined; patients that reported “very good” (score = 7) or “good” (score = 6) results were considered to be satisfied with the procedure.

Results:: Neuropathic pain and central sensitivity syndromes was significantly reduced at each visit follow up after PRF (P < 0.001, repeated measures one-factor analysis). In addition, at 3 months post-PRF, more than half of the patients achieved a successful response (≥ 60% pain reduction) and were satisfied with treatment results.

Conclusions:: CPRF stimulation under ultrasonic guided more safe for patients and clinicians. And can do in outpatients.
POST AUTHORIZATION SAFETY STUDY ON PITOLISANT (PASS-PITOLISANT) IN NARCOLEPSY: RESPONSE TO TREATMENT FROM THE ITALIAN MULTICENTER COHORT.

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Background and Aims:: 14 Italian Centers enrolled 191 narcoleptic patients in the observational PASS-pitolisant. Besides drug’s safety, the study analyzed variations of narcolepsy symptoms, depression, quality of life and disease burden.

Methods:: from PASS-Pitolisant’s 3rd Interim report we extracted detailed clinical data on patients who concluded the 1-year follow-up (FU) visit. Clinical Global Impression (CGI) for Excessive Daytime Sleepiness (EDS) and cataplexy severity were judged by sleep experts. Validated questionnaires were administered to evaluate EDS (Epworth Sleepiness Scale, ESS), depression (Beck Depression Inventory, BDI), quality of life (EQ-5D-5L) and disease burden (Functional Outcome of sleep questionnaire, FOSQ10).

Results:: of the 191 patients (76.4% narcolepsy type I and 23.6% narcolepsy type II) enrolled, 96 completed the 1-year FU visit. ESS decreased from 15.2±4.4 at baseline to 12.4±4.5 and responders (ESS≤10 or ESS decrease≥3) were 57.3%. Other main narcoleptic symptoms including cataplexy, sleep attacks, sleep paralysis and hypnagogic hallucinations ameliorated in 39.7%, 49.4%, 15.6% and 21.5% of patients, respectively. According to CGI, 87.5% of patients had improvement of EDS and 64.5% of cataplexy. Moreover, at FU visit an increase of EQ-5D-5L score (baseline: 64.7; FU:15.6±3.4), an increase of FOSQ-10 score (baseline: 13.7±3.8; FU:15.6±3.4), and no worsening of BDI score for 96.3% of patients were observed.

Conclusions:: According to PASS-Pitolisant interim report, patients recruited from the Italian centers reported improvement of narcolepsy symptoms at 1-year FU. Treatment favorably impacted on quality of life and on depressive symptoms, mitigating the burden of disease.
Background and Aims:: To investigate sleep disorders in patients with Chronic kidney disease.

Methods:: Neurological Examination and the Pittsburgh Sleep Quality Assessment Scale

Results:: The study involved 42 patients undergoing routine hemodialysis (15 women (35.7%), 27 men (64.2%)) the average age was 41.6±2.8 years. 35 patients after kidney transplantation (15 women (43%), 20 men (57%), the average age was 40.6±2.3 years. For control, 40 completely healthy people, the average age of which was 37.6±3.2 years. In the group of patients undergoing routine hemodialysis, the main complaints were: insomnia (36%), daytime sleepiness (19%), restless legs syndrome (23.8%), frequent awakenings (21.4%). In the group of patients after the transplant, complaints of difficulty in falling asleep prevailed 45.7%; 17.1% of patients complained of insomnia, and 37.1% had no problems with sleep. In the control group, only 25% of patients had problems with sleep, and this was manifested in difficulty in falling asleep. The Pittsburgh Sleep Quality Assessment Scale shows the total value for all components of the PSQI scale in the group receiving hemodialysis was 8.90±1.32 points, in the group of patients after transplantation 5.34±1.54; in the control group – 3.06±0.98 points

Conclusions:: According to the Pittsburgh Scale, sleep problems are less common in transplanted patients than in patients receiving routine hemodialysis. The transplanted patients had significantly better overall sleep quality than the patients on maintenance hemodialysis, but at the same time, their sleep was worse than that of the healthy control group.
IMPACT ON THE SLEEP OF PATIENTS WITH COVID 19 IN SELF-ISOLATION: A SYSTEMATIC REVIEW

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Background and Aims:: COVID-19 challenges medicine in numerous aspects, including the triggering and / or worsening of sleep disorders, which can both hinder the treatment of this disease and may imply the emergence of other morbidities, especially mental and cardiovascular diseases. For this reason, this systematic review was carried out with the objective of verifying the sleep behavior in self-isolated individuals as well as identifying which preventive and therapeutic measures can be used to decrease sleep disturbances.

Methods:: The author performed the data extraction in 4 different databases (PUBMED, COCHRANE, MEDLINE, SCIELO) using the terms "sleep disorders" and "COVID-19 disease" as descriptors. A total of 12 articles were found from which the titles and abstracts were read, but only 5 articles were considered in accordance with the research objectives. These were then carefully analyzed and the main considerations were compiled.

Results:: The articles alert to the importance and care with the prevention, recognition and treatment of sleep-related diseases, given that social confinement and concerns about the pandemic generate negative emotions that can predispose sleep diseases and / or mental disorders that can cause considerable damage to health.

Conclusions:: Alternatives treatment as relaxation techniques, implementation of social capital and even the use of melatonin must be established to reduce the impact of sleep disorders in the COVID-19 population.
ARTIFICIAL NEURAL NETWORKS ANALYSIS OF SLEEP FEATURES AND COGNITIVE-BEHAVIORAL PROFILE IN SLEEP-RELATED HYPERMOTOR EPILEPSY AND DISORDERS OF AROUSAL

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Background and Aims:: Increased sleep instability and reduced sleep quality are both features and promoting factors for sleep-related hypermotor epilepsy (SHE) and disorders of arousal (DOA). We aimed to compare subjective sleep quality, objective sleep features and cognitive-behavioral profile in patients with SHE and DOA.

Methods:: A total of 11 subjects with DOA (3 males mean age 32.3±10.9 years) and 12 subjects with SHE (6 males 33.5±15.2 years) were enrolled at the Sleep and Epilepsy Center of the University of Cagliari. All subjects were not taking any medications and they underwent a full-night video-polysomnography together with a broad cognitive and behavioral assessment. Subjective sleep quality was evaluated by Pittsburgh Sleep Quality Index. A data mining approach with fourth-generation Artificial Neural Networks has been used in order to discover subtle trends and associations among variables.

Results:: SHE patients reported significantly more depressive symptoms (p=0.01) and they performed significantly worse in short-term verbal memory (p=0.003) and verbal learning (p=0.002), moreover, they showed worse subjective sleep quality and objective sleep efficiency (p=0.001; p=0.004) compared to DOA patients. The artificial neural network methodology and the self-contracting map exploited the links of variables that reveal the complexity of a specific phenotype allowing to group SHE and DOA respectively.

Conclusions:: SHE is associated with decreased subjective and objective sleep quality, worse cognitive profile and depressive symptoms compared to DOA patients. These results suggest a severer sleep disruption that might be associated with heavier burden of diseases in terms of sleep-based health consequences, compared to DOA.
TWENTY-FOUR HOURS BLOOD PRESSURE PROFILE IN IDIOPATHIC REM SLEEP BEHAVIOR DISORDER

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Background and Aims:: The aim of this study is to determine whether autonomic dysfunction in idiopathic REM sleep behavior disorder (iRBD) subjects affects circadian blood pressure (BP) profile.

Methods:: We performed a cross sectional study including 22 iRBD (19 males; mean age 68.1±6.1, mean age at onset 61.7±9.2), 22 de novo drug-free subjects with Parkinson’s Disease (PD) and 22 control subjects (HC) comparable for age and sex undergoing 24-hour ambulatory BP monitoring. Prospective follow-up study evaluated the occurrence of neurodegenerative disorders in iRBD cohort.

Results:: Mean BP decrease at night was lower in iRBD (4.6±8.9% for systolic and 9.1±8.1% for diastolic BP; p=.001 and p=.003 respectively) than HC. The non-dipping status was more frequent in iRBD subjects (72.7% for systolic and 54.5% for diastolic BP; p=.001 and p=.01 respectively) than HC. Inverted dipping was found in 22.7% for systolic (p=.048) and 4.5% for diastolic BP in iRBD. Non dipping status was not associated with differences in gender, age, disease duration, age at onset, UPDRS score, presence of antihypertensive therapy and polysomnographic measures. Patients with de novo PD showed comparable daytime and nighttime BP profile compared to iRBD. Sub-analysis considering only subjects without antihypertensive therapy (13 iRBD, 12 PD) showed the same results(Table1). At follow up (mean 5.2±1.9 years) no differences in BP profile at baseline were found between converters (n=7) and non-converters(table2).
Table 1. Ambulatory blood pressure monitoring

<table>
<thead>
<tr>
<th></th>
<th>iRBD</th>
<th>PD</th>
<th></th>
<th>non hypertensive iRBD (n=13)</th>
<th>non hypertensive PD (n=12)</th>
<th></th>
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<tbody>
<tr>
<td>Mean Daytime SBP</td>
<td>128.8±16.3</td>
<td>125.6±11.2</td>
<td>ns</td>
<td>125.4±12.4</td>
<td>124.7±8.9</td>
<td>ns</td>
</tr>
<tr>
<td>Mean Daytime DBP</td>
<td>75.2±8.1</td>
<td>76.4±9.1</td>
<td>ns</td>
<td>74.3±8.1</td>
<td>76.6±9.0</td>
<td>ns</td>
</tr>
<tr>
<td>Mean Nighttime SBP</td>
<td>122.8±20.2</td>
<td>118.3±12.1</td>
<td>ns</td>
<td>121.1±18.1</td>
<td>118.7±11.2</td>
<td>ns</td>
</tr>
<tr>
<td>Mean Nighttime DBP</td>
<td>68.4±9.7</td>
<td>68.5±10.5</td>
<td>ns</td>
<td>68.3±9.6</td>
<td>70.6±9.6</td>
<td>Ns</td>
</tr>
<tr>
<td>Absent systolic dipping</td>
<td>72.7%</td>
<td>72.7%</td>
<td>ns</td>
<td>69.2%</td>
<td>83.3%</td>
<td>Ns</td>
</tr>
<tr>
<td>Absent diastolic dipping</td>
<td>63.8%</td>
<td>54.5%</td>
<td>ns</td>
<td>69.2%</td>
<td>75.0%</td>
<td>Ns</td>
</tr>
<tr>
<td>Reverse systolic dipping</td>
<td>22.7%</td>
<td>13.6%</td>
<td>ns</td>
<td>30.8%</td>
<td>8.3%</td>
<td>Ns</td>
</tr>
<tr>
<td>Reverse diastolic dipping</td>
<td>4.5%</td>
<td>4.5%</td>
<td>ns</td>
<td>7.7%</td>
<td>0%</td>
<td>Ns</td>
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<tr>
<td>Mean systolic dip</td>
<td>6.1±11.6</td>
<td>7.3±9.0</td>
<td>ns</td>
<td>1.4±12.4</td>
<td>6.0±7.6</td>
<td>Ns</td>
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<tr>
<td>Mean diastolic dip</td>
<td>6.7±6.3</td>
<td>8±6.3</td>
<td>ns</td>
<td>6.1±6.9</td>
<td>6.1±5.5</td>
<td>Ns</td>
</tr>
</tbody>
</table>

Abbreviation: SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BP is expressed in mmHg
<table>
<thead>
<tr>
<th>Variables</th>
<th>iRBD converters</th>
<th>iRBD non-converters</th>
<th>P</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>68.00±6.37</td>
<td>68.21±6.2</td>
<td>.943</td>
</tr>
<tr>
<td>Male sex</td>
<td>85.7%</td>
<td>86.7%</td>
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</tr>
<tr>
<td>Mean age of onset (years)</td>
<td>59.4 ± 13.2</td>
<td>62.8 ± 7.0</td>
<td>.437</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>13.8 ± 8.2</td>
<td>11.6 ± 6.8</td>
<td>.551</td>
</tr>
<tr>
<td>AHI</td>
<td>2.7 ± 3.07</td>
<td>3.53 ± 5.59</td>
<td>.675</td>
</tr>
<tr>
<td>ODI</td>
<td>3.7 ± 4.5</td>
<td>1.4 ± 4.0</td>
<td>.273</td>
</tr>
<tr>
<td>UPDRS</td>
<td>11.0 ± 6.2</td>
<td>2.1 ± 2.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hypertension in treatment</td>
<td>28.6%</td>
<td>40.0%</td>
<td>1</td>
</tr>
<tr>
<td>Alpha/Betablockers treatment</td>
<td>28.6%</td>
<td>26.7%</td>
<td>1</td>
</tr>
<tr>
<td>Current or ex-smoker</td>
<td>14.3%</td>
<td>0%</td>
<td>.318</td>
</tr>
<tr>
<td>Abnormal DAT-SPECT</td>
<td>57.1%</td>
<td>25.1%</td>
<td>.326</td>
</tr>
<tr>
<td>MMSE</td>
<td>29.4±0.9</td>
<td>27.0±5.2</td>
<td>.207</td>
</tr>
<tr>
<td>Daytime SBP (mmHg)</td>
<td>128 ± 16</td>
<td>131 ± 19</td>
<td>.726</td>
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<tr>
<td>Daytime DBP (mmHg)</td>
<td>72 ± 6</td>
<td>77 ± 9</td>
<td>.225</td>
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<tr>
<td>Nighttime SBP (mmHg)</td>
<td>127 ± 22</td>
<td>121 ± 21</td>
<td>.561</td>
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<tr>
<td>Nighttime DBP (mmHg)</td>
<td>69 ± 19</td>
<td>68 ± 10</td>
<td>.956</td>
</tr>
<tr>
<td>Mean systolic dip</td>
<td>1.1±12.9</td>
<td>8.4±10.6</td>
<td>.221</td>
</tr>
<tr>
<td>Mean diastolic dip</td>
<td>4.1±6.5</td>
<td>8.1±5.9</td>
<td>.197</td>
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<tr>
<td>Absent systolic dipping</td>
<td>57.1%</td>
<td>73.3%</td>
<td>.630</td>
</tr>
<tr>
<td>Absent diastolic dipping</td>
<td>57.1%</td>
<td>53.3%</td>
<td>1</td>
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<tr>
<td>Reverse systolic dipping</td>
<td>42.9%</td>
<td>13.3%</td>
<td>.274</td>
</tr>
<tr>
<td>Reverse diastolic dipping</td>
<td>14.3%</td>
<td>0%</td>
<td>.318</td>
</tr>
</tbody>
</table>

Abbreviation: UPDRS: Unified Parkinson's Disease Rating Scale; MMSE: Mini mental Status Examination; AHI: Apnea hypopnea Index; ODI: oxygen desaturation index
Conclusions:: 24-hour BP control was impaired in iRBD with reduced amplitude of nocturnal dipping and increased frequency of non-dipping status, similarly to de novo PD. This could affect cardiovascular morbidity and mortality in iRBD.
PREVALENCE OF SLEEP AND ANXIETY DISORDERS ON BATIK WORKERS WITH LOW BACK PAIN IN YOGYAKARTA, INDONESIA

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¹Universitas Gadjah Mada, Neurology, Yogyakarta, Indonesia, ²Universitas Gadjah Mada, Faculty Of Medicine, Public Health, And Nursing, Yogyakarta, Indonesia

Background and Aims:: Yogyakarta is one of Indonesia’s batik producer regions, one of which is located in Lendah, Kulon Progo where the batik industry is the main source of income. Throughout the process of batik production, batik workers have to do repetitive movements with non-ergonomic posture for the long-hour shifts. This puts them at risk of getting any neuromuscular and psychological problems. In Lendah, 70.4% of its batik workers suffer low back pain. This condition may affect their productivity at work, their economics, and their quality of life. The purpose of this research is to know the prevalence of sleep and anxiety disorders on batik workers with low back pain in Kulon Progo, Yogyakarta, Indonesia.

Methods:: This research is using a cross-sectional method and it takes place in batik-producing centers in Kulon Progo, Yogyakarta. The number of subjects in this research is 26 people. This research uses the Indonesian version of the Insomnia Severity Index and Hamilton Rating Anxiety Scale (HARS) questionnaire to determine sleep disorders and anxiety disorders.

Results:: The result shows that 5 out of 26 subjects (19.2%) suffer sleep disorders and 4 out of 26 subjects (15.4%) suffer anxiety disorders. The majority of subjects who suffer from sleep and anxiety disorders are workers with a range of age 25-34 years old, worked for less than 6 years, work in the stamping section, and work for less than 8 hours a day.

Conclusions:: The prevalence of sleep and anxiety disorder in batik workers with low back pain in Kulon Progo, Yogyakarta is 19.2% and 15.4%
Background and Aims:: Hypersomnolence is a risk factor of ischemic stroke (IS), as well as one of its complications. We analyzed literature sources to study existing methods and neurotransmitters for diagnosing hypersomnolence in acute IS, and to assess the possibility and necessity of their use in this group of patients.

Methods:: We reviewed 64 publications taken out from the databases PubMed, Embase, Frontiers, ResearchGate.

Results:: Currently, for the clinical and instrumental assessment of hypersomnolence disorders, questionnaires (ESS, SSS, PSQI), sleep diary, MSLT, PSG, actigraphy are used. Each method has its own pros and cons. They all complement each other, making it possible to compose the most complete picture. The main criteria for choosing a method – the ability to perform a specific study in a hospital, and the patient's ability to postpone the study / fill out questionnaires. GABA, adenosine, glutamate, norepinephrine, serotonin, acetylcholine were mentioned as laboratory biomarkers. In the context of our search for hypersomnia biomarkers in IS, glutamate, GABA, and acetylcholine seem to be the most promising. The influence of most neurotransmitters on the regulation of sleep and wakefulness has been studied only experimentally. The gradual accumulation of deeper knowledge about the neurochemistry of the sleep-wake cycle will lead to the development of new laboratory tests, as well as new treatments for patients with post-stroke hypersomnolence.

Conclusions:: To determine the optimal diagnostic algorithm for hypersomnolence in patients in the acute period of stroke, it is necessary to study with the rational use of the considered methods.
Background and Aims:: autoimmune encephalitis (AE) is frequently associated with manifold sleep disturbances, but limited information on sleep structure is available. Polysomnographic (PSG) features were analyzed in a 32-year-old woman with AE manifesting with subacute behavioral anomalies, confusion, aphasia and focal left temporal seizures. Anti-thyreoperoxidase antibodies were detected on cerebrospinal fluid.

Methods:: overnight PSG was recorded 10 days after admission. Standardized sleep scoring (macrostructure), enriched by cyclic alternating pattern (CAP) analysis (microstructure) was performed and compared to age-matched healthy sleepers (HS).

Results:: PSG showed sleep fragmentation (30 awakenings), reduction of sleep efficiency (81%), curtailment of REM sleep (16%). The most relevant deviations were noticed at the microstructural level, with reduction of sleep instability (CAP rate 16.5% vs 33% in HS), flat nocturnal distribution and reduced length of CAP cycles, shorter A phases and prevalence of CAP subtypes A2. Diffused paroxysmal discharges were observed during NREM and REM sleep. Notably most CAP cycles were triggered by epileptiform discharges, however they rarely structured into CAP sequences.

Conclusions:: to the best of our knowledge this is the first PSG analysis of an AE in the subacute phase evaluating microstructural data. Reduction of CAP oscillations and anomalies in their duration and ultradian distribution were the main findings, in contrast with the commonly observed increase of CAP rate in epileptic patients during sleep. Recent evidences described impairment of CAP parameters in various neurodegenerative disorders. The role of sleep in the entanglement between epilepsy, inflammation and evolving neurodegeneration in AE is discussed.
UNDERESTIMATED SLEEP BREATHING DISORDERS IN A COHORT OF PATIENTS ADMITTED TO POST-COVID19 FOLLOW-UP PROGRAM: A SINGLE CENTER EXPERIENCE

Marco Cesare Angeli¹, Francesco Rausa¹, Elia Satta², Marcello Luigi Salvatelli¹, Irene Pollara¹, Clara Rapina¹, Marina Aiello², Pier Anselmo Mori², Raffaele D'Ippolito³, Emanuela Burlone³, Veronica Alfieri³, Maria Majori⁴, Carlotta Mutti¹, Liborio Parrino¹
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Background and Aims:: Sleep Breathing Disorders (SBD) have been suggested as potential risk factors for critical Covid19. We explored the prevalence of undiagnosed SBD in a cohort of > 200 adult patients admitted to the multidisciplinary follow-up program for Covid19 at Parma Hospital. Functional outcomes and prognosis will be compared between obstructive sleep apnea (OSA) versus non-OSA patients.

Methods:: In the follow-up program patients considered at high risk for SBD, measured through validated questionnaires (STOP-BANG, Epworth Sleepiness Scale) supported by the physician’s evaluation, are sent to our Sleep Disorders Centre for nocturnal cardiorespiratory recording.

Results:: So far 94/150 patients (mean age 59.3 +/- 11.5, 59.6% male, mean BMI 32.6 +/-6.95) have been admitted to our Sleep Disorders Center. Overall 68.1% (64/94) were affected by OSA divided in: 38/94 (40.4%) mild (apnea hypopnea index - AHI 5-15/h), 9 (9.6%) moderate (AHI 15-30/h) and 18 (19.1%) severe (AHI>30/h). 9/94 obese patients (9.6%) presented sleep-related hypoxemia suspected for obesity hypoventilation syndrome. 22/94 (23.4%) showed a periodic limb movements disorder.

Conclusions:: Our preliminary results identified a high rate of undiagnosed sleep-related breathing and movement disorders in a large adult cohort of patients with recent Covid19. Disease severity and clinical outcomes between undiagnosed OSA versus non-OSA patients will be detailed. Sleep evaluation enriches post-Covid19 follow-up investigation, providing highly informative in patients complaining of excessive daytime sleepiness.
PREDICTORS ASSOCIATED WITH VERY SEVERE OBSTRUCTIVE SLEEP APNEA [AHI>60 EVENTS PER HOUR] AMONG SLEEP CENTER PATIENTS IN MONGOLIA

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1General hospital for state special servants, Sleep Center, Ulaanbaatar, Mongolia, 2Mongolian National University of Medical Sciences, Neurology, Ulaanbaatar, Mongolia

Background and Aims:: Obstructive sleep apnea (OSA) is a common condition characterized by repetitive obstruction of the upper airway during sleep with resultant episodic hypoxia and arousal. The presence of OSA is determined from Apnea-Hypopnea Index (AHI). Our goal is to characterize the demographics, clinical and sleep characteristics of very severe OSA (vsOSA). Moreover, we aimed to analyze predictive factors for OSA.

Methods:: In this cross-sectional, prospective, hospital-based study patients were divided of AHI < 60, and AHI >60. Demographic, anthropometric, clinical and polysomnographic (PSG) variables included for the analysis were: age, weight, BMI, neck and abdominal circumference, Malanpatti’s score, Tonsil grade, blood pressure (BP), oxygen saturation (SpO2) and selected PSG indicators. Data analyses were conducted with SPSS version 26.0.

Results:: Male (105) were slightly more than women (102) out of remaining 207. Mean age was 48.7±12.7. 70% of had higher education and live in the Ulaanbaatar. Patients divided into 2 groups of AHI<60 (157) and AHI>60 (50). Meantime women tend to have AHI<60 (62%), while man have severe (90%) (p<0.0001). Most of anthropometric; vital measurements were significantly increased in AHI>60 group (p<0.0001). All sleep questionnaires showed decreased sleep quality and day time sleepiness in AHI>60. PSG variables showed decreased sleep efficiency. (p<0.0001). Between possible risk factors and the AHI were gender, SpO2 min, neck circumference, and PSQI questionnaire showed high correlation.

Conclusions:: In Mongolia 90% of male OSA patients have AHI>60, younger obese men. Increased abdominal and neck circumference, lower level of minimal and maximum SpO2 had significant risk factor for vsOSA.
OBSTRUCTIVE SLEEP APNEA (OSA) DETECTION SYSTEM BASED ON FAST FOURIER TRANSFORM (FFT) ALGORITHM ON ELECTROCARDIOGRAM

Rifaldy Fajar, Prihantini Jupri, Sahnaz Putri
Yogyakarta State University, Computational Biology And Medicine Laboratory, Sleman, Indonesia

Background and Aims:: In this study, an Obstructive Sleep Apnea (OSA) disease detection system was created using the RR interval parameter. The design of this detection system uses backpropagation Artificial Neural Network (ANN) which is implemented using MATLAB software as a method in the classification of OSA determination.

Methods:: The steps taken to design an OSA disease detection system in this study include data collection, feature extraction, ANN training, ANN testing, and performance determination. The feature extraction stage is performed using the Fast Fourier Transform (FFT) mathematical algorithm process. The result of feature extraction is then carried out ANN training using 10% of the entire data and ANN testing using 90% of the total data. To get the best performance results, variations in segment length features, variations in OSA definition features, and variations in frequency composition features are performed.

Results:: The best performance results in this OSA disease detection system design are features that use a combination of frequency components 2, 5, and 6 with an OSA definition of 5% in the 90-segment length. This is shown from the results of ANN performance in the form of specialization, sensitivity, and best accuracy, with successive values of 79.3%, 84.6%, and 81.6%.

Conclusions:: A system design has been made to detect OSA. The feature used in this detection system is the RR interval feature that has been transformed using the Fast Fourier Transform operation. Based on the results of performance calculations, all values indicate a number exceeding 75% so that a system that can be said to be good in detecting is obtained.
PHASE AND AMPLITUDE CORRELATIONS CHANGE WITH DISEASE PROGRESSION IN IDIOPATHIC RAPID EYE-MOVEMENT SLEEP BEHAVIOR DISORDER PATIENTS

Dario Arnaldi¹, Monica Roascio², Pietro Mattioli¹, Andrea Donniagio¹, Francesco Famà¹, Laura Giorgetti¹, Nicola Girtler¹, Beatrice Orso¹, Andrea Brugnolo¹, Matteo Pardini¹, Silvia Morbelli², Flavio Nobili³, Gabriele Arnulfo²

¹University of Genoa, Department Of Neuroscience (dinogmi), Genoa, Italy, ²UNIGE, Department Of Informatics, Bioengineering, Robotics And System Engineering (dibris), Genoa, Italy, ³University of Genoa and IRCCS Ospedale Policlinico San Martino, Department Of Health Science (dissal), Genoa, Italy

Background and Aims:: Increased phase synchronization in EEG bands is thought to reflect the activation of compensatory mechanisms of cognitive decline in people with neurodegenerative diseases. Here we investigated whether altered large-scale couplings of brain oscillations could be linked to the balancing of cognitive decline in a longitudinal cohort of people with Idiopathic Rapid eye-movement sleep Behavior Disorder (iRBD).

Methods:: High-density EEG (HD-EEG), presynaptic dopaminergic imaging, clinical and neuropsychological data have been acquired in 18 patients (17 males, 70.6.8 years) with iRBD at two time-points (time interval 24.2 ± 5.9 months). HD-EEG power distribution, orthogonalized amplitude correlation and weighted phase lag index have been quantified at both time-points and correlated with clinical, neuropsychological and imaging data.

Results:: Four patients phenoconverted at follow-up (three parkinsonism and one dementia). At group level, neuropsychological scores decreased over time, without reaching statistical significance. However, alpha phase synchronization increased, and delta amplitude correlations decreased significantly at follow-up compared to baseline. Both large-scale network modulation significantly correlated with neuropsychological scores but not with sleep quality indices or presynaptic dopaminergic imaging data.

Conclusions:: These results suggest that increased alpha phase-synchronization and reduced delta amplitude correlation may be considered as electrophysiological signs of an active compensatory mechanism of the cognitive impairment in people with iRBD. Large-scale functional modifications may be helpful biomarker in the characterization of prodromal stages of alpha-synucleinopathies.
SLEEP DISORDERS AS A PREDICTOR OF PARKINSON'S DISEASE IN UZBEK NATIONALITY.

Bakhrom Amonov, Rustambek Matmurodov, Eldor Abdukodirov, Khanifa Khalimova
Tashkent medical academy, Neurology, Tashkent, Uzbekistan

Background and Aims:: One of the earliest and most significant non-motor disorders in Parkinson's disease (PD) is sleep disturbance. To study sleep disturbance in PD in persons of Uzbek nationality.

Methods:: We examined 106 patients with PD (56 men and 51 women aged 56.09±10.9 years) and 10 healthy individuals matched by sex and age. The duration of the disease was 5.35±5.5 years, the stage of the disease according to the Hoehn-Yahr scale was 2.7±0.9.

Results:: The obtained results show that in 92 patients (86.75%) sleep disorders of the type of hyposmia and hypersomnia were observed. After 4–5 years, these patients developed a triad of symptoms such as bradykinesia, muscle rigidity and resting tremor. In 13 patients (12.2%), the disease began with movement disorders. Of 106 patients, 54 patients began to have sleep disturbances and changes in human character after a year, and motor disturbances developed very slowly. The long-term stage of the disease in these patients was 2.6 ± 0.6 years. In 52 patients, after 1/2 year, bradykinesia and an increase in the tone of the plastic type were observed, and the treatment of diseases was rapidly aggravated. The long-term stage of the disease in these patients was 1.5 ± 0.7 years.

Conclusions:: It should be noted above that the clinic and course of Parkinson's disease non-moving disorders, such as sleep disturbances, the characteristics and characteristics of the disease, depend on the duration and stage of the disease. Disorders are the main preclinical predictor of PD development, which requires timely diagnosis and treatment.
INFLUENCE OF COVID 19 IN MEDICAL STUDENTS’ SLEEPING CIRCLE

Francinny Kelly¹, Vhirginea Helena De Oliveira Staut Federle¹, Monaí Oliveira², Fernanda Garcia Passos³, Marcelo Hettwer⁴
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Background and Aims:: The correlation between COVID 19 and its impact in the people's lifestyle are still very new. However it is already possible to notice that it have been affecting human behavior and their way of living. The aim of this study is to evaluate the correlation of the COVID pandemic and how it affected medical students’ sleep quality.

Methods:: One hundred-fifty-three medical students from first to fifth year, volunteered to participate through an online questionnaire. Written approval was granted. The students answered a question (Q1) about the quality of their sleep. Q1: “During the pandemic, did you have any change on your sleep?”

Results:: Sleeping more but with lower quality: 34,6%; Sleeping more and with better quality: 22,2%; Sleeping less and lower quality: 20,3%; Sleeping less but with the same quality: 11,1%; No changing on the sleep: 11,8%

Conclusions:: The changes in lifestyle during the pandemic were significant, especially for medical students that have had all their schedules changed and in some cases, have been even fighting against COVID-19. As a result of these changes, it’s possible to notice that the amount and the quality of sleep have both been impacted during the COVID-19 pandemic. It could have been caused by a multitude of causes, ranging from emotional disorders to changes in the of the students’ quality of life.
A DATA DRIVEN APPROACH TO NEUROPSYCHOLOGICAL FEATURES IN ISOLATED REM BEHAVIOR DISORDER: A FOLLOW-UP INVESTIGATION.

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Background and Aims:: Isolated REM Behavior Disorder (iRBD) predates the insurgence of neurodegeneration by many years. Therefore, the neuropsychological evaluation in this condition is crucial. This study has two main goals: (1) to provide a neuropsychological profiling of a large cohort of iRBD subjects based on a data driven approach using Latent Class Analysis (LCA); (2) to evaluate neuropsychological trajectories from baseline to follow-up for each latent class.

Methods:: 289 iRBD patients at baseline (85.5% males, mean age: 67.58±7.69 years) underwent neuropsychological assessment. A subsample of 66 patients (86.4% males, mean age: 69.53±7.60 years) underwent a neuropsychological evaluation at follow-up (36.15±30.24 months). LCA was carried out to identify iRBD subtypes according to baseline neuropsychological scores, categorized into the following cognitive domains: global cognition, language, short-term memory, long-term memory (LTM), executive function (EF), and visuospatial abilities.

Results:: The most parsimonious model identified 3 latent classes. Groups were labeled as follows: class 1, moderately impaired (n=44); class 2, severely impaired (n=83); class 3, slightly impaired (n=162). EF and LTM significantly worsen (p<0.01) for all 3 classes over time. Considering EF, class 1 exhibited the greatest decrease in this cognitive domain compared to the other classes. Accordingly, class 1 showed the greatest increase in Mild Cognitive Impairment (MCI) frequencies from baseline (50.0%) to follow-up (58.3%).

Conclusions:: Our study identified 3 different cognitive phenotypes of iRBD. This identification might help in predicting different trajectories of neuropsychological performances and MCI diagnosis.
COGNITIVE-BEHAVIORAL INTERVENTIONS FOR THE ADHERENCE TO POSITIVE AIRWAY PRESSURE THERAPY: A META-ANALYSIS.

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Background and Aims:: The first-line treatment of obstructive sleep apnea (OSA) is positive airway pressure therapy (PAP). In this context, adherence is widely recognized as problematic with mean adherence rates ranging between 46% to 89% limiting the effectiveness. Cognitive and behavioral interventions (CB) are promising for promoting adherence to PAP therapy. Our aim is to quantify the efficacy of CB interventions (Cognitive-Behavioral Therapy for Insomnia, Motivational Enhancement Therapy, Motivational Interview Nurse Therapy, Stage Matched Care and SCIP-PA Tailored Intervention) on PAP adherence in OSA patients through a meta-analysis.

Methods:: A systematic search of the relevant literature was performed by two independent researchers in Pubmed, Psychinfo, Cinhal, Embase, Scopus, and Medline up to December 2020. Including Randomized Controlled Trial (RCT) with CB interventions and PAP adherence as principal outcome, we implement a classical meta-analysis design with follow-up duration as covariate.

Results:: 10 RCT were selected (N intervention=466; N controls=471). The results suggest that the CB interventions’ effects on PAP adherence is medium (RE model d=0.44, CI 0.13-0.75). The mean usage for the control group was 3.46±2.15 hours, and 4.21±2.15 hours for the intervention group. No effect of follow-up duration was found (p=0.96).

Conclusions:: This meta-analysis provides evidence of a medium positive effect of CB intervention compared to the control group, on PAP adherence. These findings suggest that OSA patients with PAP therapy might receive beneficial effects from CB intervention, however there is a need for further investigation in this field.
SYMPTOMS AND RISK OF OBSTRUCTIVE SLEEP APNEA IN THE MONGOLIAN POPULATION: A NATION-WIDE ANALYSIS FROM THE MON-TIMELINE STUDY

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Background and Aims:: The prevalence of obesity is dramatically increasing in Mongolia. Obese people have a higher risk for non-communicable diseases and Obstructive Sleep Apnea (OSA) syndrome. There is no data on the prevalence of OSA in the Mongolian population.

Methods:: We evaluated the risk of OSA using data from the population-based Mon-Timeline cohort (18 - 65 years of age). The risk of OSA syndrome was evaluated using the Berlin questionnaire, which consists of three categories (category 1: snoring and witnessed apneas; category 2: daytime sleepiness; and category 3: high blood pressure/obesity). Those who met any two of the three categories were considered at high risk for OSA syndrome.

Results:: In this cross-sectional study, a total of 1405 people - with a mean age of 42 ± 14.3, of which 42.5% were males - completed the questionnaire. Among them, 24.4% was classified as being at higher risk for OSA syndrome. Furthermore, 41.7% of the participants reported snoring, of which 39.3% responded that their snoring bothers other people. The prevalence of people with a higher risk for OSA syndrome was found to increase with age: notably 6.7%, 28.3% and 39.4% for age groups <30, 30 - 50, and >50 years, respectively. There were no differences between gender and education throughout the OSA risk categories.

Conclusions:: Based on a representative sample population, we conclude that OSA is prevalent and common among the Mongolian population.
RESTLESS LEGS SYNDROME AS A PREDICTOR OF SLEEP, FATIGUE, AND MENTAL HEALTH IN PATIENTS WITH CARDIOVASCULAR DISEASE

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Background and Aims:: Restless legs syndrome (RLS) is a neurological disorder which is associated with sleep disruption and poor quality of life. It is often found to be a comorbid condition in individuals having cardiovascular diseases (CVD). The purpose of the current study was to find out the frequency of RLS among CVD patients and to examine sleep, fatigue, and mental health in patients with and without RLS.

Methods:: It was a cross-sectional study. A convenience sample of 200 CVD patients with age range between 35-65 years (55.49±7.67) was selected from different hospitals of Lahore, Pakistan. The patients completed the fatigue severity scale (FSS), general health questionnaire12 (GHQ-12), sleep problems scale and restless legs syndrome scale.

Results:: The results indicated that 14% of the CVD patients had RLS. Fatigue, sleep, and mental health was worse in patients having comorbid RLS as compared to the ones without RLS. General linear model showed RLS, BMI, and CVD duration as significant predictors (p<.05) of poor sleep, fatigue, and deteriorated mental health in patients. Being female, increasing age and obesity were associated with an increased likelihood of RLS.

Conclusions:: RLS may affect patients having CVD affecting their treatment outcomes negatively. Screening the CVD patients for RLS could prove to be beneficial by reducing complications. The awareness of the associations indicated in this study among these variables might help health care providers in treating patients with CVD, sleep disorders or psychological problems to recognize potential contributing factors and to address those causes accordingly.
ASSOCIATION BETWEEN SUBJECTIVE–OBJECTIVE DISCREPANCY OF SLEEPING TIME AND HEALTH-RELATED QUALITY OF LIFE: A COMMUNITY-BASED POLYSOMNOGRAPHIC STUDY

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¹Gachon University Gil Medical Center, Psychiatry, beon-gil, Namdong-daero, Namdong-gu, Incheon, Korea, Republic of, ²Gachon University College of Medicine, Preventive Medicine, Incheon, Korea, Republic of

Background and Aims:: This study aims to investigate the existence of a difference in QOL between individuals with and without significant subjective–objective discrepancy (SOD) of total sleep time (TST).

Methods:: From the Sleep Heart Health Study (SHHS) 2, a total of 2,540 individuals who had completed polysomnography, a morning sleep survey, and the 36-item Short-Form Health Survey (SF-36) were included in the analyses. The participants were classified as normoestimators (estimation of TST < ± 60 min), underestimators (underestimation of TST ≥ 60 min), or overestimators (overestimation of TST ≥ 60 min). The standardized SF-36 QOL scores were compared between the 3 groups. An adjusted partial correlation analysis was conducted between SOD and QOL.

Results:: Of the 2540 participants, 1617 (63.7%), 433 (17.0%), and 490 (19.3%) were assigned to the normo-, under-, and overestimator groups, respectively. The bodily pain and social functioning components of the SF-36 score were significantly lower in the underestimators than in the normoestimators, whereas the physical functioning component was significantly lower in the overestimators than in the normoestimators. The absolute value of SOD in TST showed a significant negative correlation with physical and mental components of the SF-36.

Conclusions:: QOL was significantly better in the normoestimator than in the other groups, and linearly correlated with the absolute value of SOD. This study suggests that highly prevalent positive and negative sleep misperception in a community population can be a potential marker for poor QOL and potential co-morbidities.
SEX RELATED DIFFERENCES IN INFLAMMATION MARKERS IN ADULT PATIENTS WITH OBSTRUCTIVE SLEEP APNEA.

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Background and Aims:: Obstructive Sleep Apnea (OSA) is the highest prevalent sleep-related breathing disorder. Its link to inflammation and metabolic derangement is well known, as is its role as vascular risk factor. Men and women may show different symptom presentation and response to therapy. In this study we aimed to valuate sex-related differences in inflammatory status and their relationship with OSA severity.

Methods:: 110 consecutive subjects referred to the outpatient Sleep Disorder Service of the Respiratory Medicine Department, San Marino Hospital, were considered. Inclusion criteria were a diagnosis of moderate or severe OSAS and age range 45-80 years. Subjects with inflammatory conditions were excluded. All subjects underwent a polygraphic study and a blood draw for inflammatory markers.

Results:: Fifty-one of our subjects were females and 72 were affected by severe OSA. We created a 4-level categorical variable (moderate OSA, males; severe OSA, males; moderate OSA, females; severe OSA, females), where significant differences for interleukin-6 (IL-6) and C-reactive protein (CRP) emerged. The pairwise comparison for estimated marginal means of IL-6 and CRP showed a significant difference in IL-6 levels with a significant ascending trend (p=0.045) from females with moderate OSAS to males with severe OSAS. Similarly, we observed a significant trend (p=0.0001) for CRP levels from males with moderate OSAS to females with severe OSAS.

Conclusions:: OSA and inflammation are strongly related and both conditions are associated with vascular morbidity. Men and women may differ in OSA presentation and in inflammatory status, suggesting a personalized clinical approach.
Background and Aims:: Solriamfetol, a dopamine/norepinephrine reuptake inhibitor, is approved (EU/US) to treat excessive daytime sleepiness (EDS) in adults with narcolepsy (75-150 mg/day) or obstructive sleep apnoea (OSA) (37.5-150 mg/day). This study characterised patients with narcolepsy starting solriamfetol and prescribers’ rationales for initiating treatment.

Methods:: This retrospective chart review enrolled US-based physicians prescribing solriamfetol. Solriamfetol initiation was de novo (no prior EDS medication), transition (switched/switching from existing EDS medications), or add-on (adding to current EDS medication).

Results:: Twenty-three physicians entered data from 70 patients with narcolepsy (type 1, n=24; type 2, n=46; mean±SD age, 40±11 years; 57% female; 31% obese [BMI≥30]; 6 also had OSA). EDS was primarily moderate (59%) or severe (36%). Common comorbidities were migraines (17%), depression (14%), and cardiovascular disorders (14%). Solriamfetol initiation was de novo (n=19, 27%), transition (n=31, 44%), or add-on (n=20, 29%). Most transitioning (29/31, 94%) patients were taking 1 EDS medication, typically wake-promoting agents (22/31, 71%). Add-on patients were primarily taking 1 EDS medication (16/20, 80%), most frequently sodium oxybate (11/20, 55%). Solriamfetol’s efficacy was the primary reason prompting discussions to prescribe de novo (12/19, 63%); need for improved efficacy/augmenting effects of other medications was the primary reason for transitioning (18/31, 58%) and add-on (19/20, 95%). At data collection, 63 (90%) patients were on a stable solriamfetol dose. The most common reasons for discontinuing solriamfetol were lack of efficacy (n=3) and side effects (n=3).

Conclusions:: Efficacy and need for improved efficacy over existing medication(s) were key considerations for physicians prescribing solriamfetol to patients with narcolepsy.
Background and Aims:: Solriamfetol is a dopamine/norepinephrine reuptake inhibitor approved (EU/US) to treat excessive daytime sleepiness (EDS) in adults with narcolepsy (75-150 mg/day) or obstructive sleep apnoea (OSA) (37.5-150 mg/day). Given its clinical availability, this study characterised real-world dosing and titration with solriamfetol.

Methods:: This descriptive study included a quantitative retrospective patient chart review among US-based physicians prescribing solriamfetol for patients with EDS associated with narcolepsy or OSA. Initiation strategies were classified as de novo (no prior EDS medication), transition (switched/switching from existing EDS medications to solriamfetol), or add-on (adding solriamfetol to current EDS medication).

Results:: Physicians (n=23) entered data from 70 patients with narcolepsy (24/70 type 1; 46/70 type 2; mean±SD age, 40±11 years; 57% female; 6 also had OSA). EDS was mainly moderate (59%) or severe (36%). Nineteen patients (27%) initiated de novo, 31 (44%) transitioned, and 20 (29%) were add-on. Most patients (86%) started solriamfetol at 75 mg and were stable at 150 mg (76%). Most (67%) had 1 dose adjustment; median (range) time to a stable dose was 14 (1-60) days. EDS severity (44% of patients) was frequently considered when titrating. Fourteen of 22 (64%) transitioning from a wake-promoting agent (WPA) stopped it abruptly while 5/9 (56%) using stimulants tapered off. Physicians were likely (n=33, 47%) or very likely (n=30, 43%) to recommend their approach for similar patients.

Conclusions:: In a real-world study, most physicians prescribing solriamfetol to patients with narcolepsy started at 75 mg, tapered stimulants, abruptly discontinued WPAs, and made 1 dose adjustment.
SLEEP AND PREGNANCY

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Background and Aims:: The occurrence of anatomical, physiological, hormonal and psychological changes during pregnancy can be responsible for sleep alterations that can affect maternal and fetal health state of the pregnant woman and the well-being of the fetus. In this respect, an increased prevalence of obstructive sleep apnea syndrome (OSAS), restless legs syndrome (RLS) and insomnia have been demonstrated.

Methods:: Fifty consecutive pregnant women aged 28.47±3.75 were selected and evaluated during the three trimesters. Validated approaches for the diagnosis of OSAS, RLS and insomnia were used. In the presence of one of these conditions, their severity was determined also by using specific scales.

Results:: During the study period, a high prevalence of OSAS, RLS and insomnia was evidenced. Furthermore, in subjects who complained of disorders in the early periods of pregnancy, there was a progressive increase in the severity of symptoms.

Conclusions:: OSAS and RLS are associated with an increased prevalence of pre-eclampsia and diabetes. In particular, the risk of hypertension in pregnancy, negatively influences intrauterine growth and increases the risk of caesarean delivery. Insomnia in pregnancy greatly increases the risk of postpartum depression. Despite the well-documented complications resulting from the presence of sleep disorders in particular OSAS, RLS and insomnia during pregnancy, to date sleep alterations in this particular condition are not adequately taken into account. Common sleep disorders such as OSAS, RLS, insomnia have a high prevalence in pregnancy, particularly during the third trimester with important effects on the outcome of pregnancy itself and the puerperium. Hence, the importance of promoting adequate screening aimed at an early identification.
THE PSYCHOLOGICAL IMPACT OF SLEEP QUALITY ON HEALTH CARE WORKERS DURING COVID-19 IN JORDAN

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Background and Aims:: Sleep quality is a key aspect of the overall psychological health. Sleep quality can affect mental health in many aspects, causing major psychological disorders, such as: depression and anxiety. Objectives: to assess the overall psychological impact of sleep quality on health care providers in Jordan during COVID-19 pandemic.

Methods:: This is a descriptive cross-sectional multicenter hospital-based study conducted in Jordan from the period of 2/7/2021 to 12/7/2021. 418 participants were included in the study. Data collection was done online via Google form. A questionnaire was used containing 4 validated scales, the insomnia severity index (ISI), Epworth sleepiness scale (EPS), generalized anxiety disorder-7 (GAD-7), patient health questionnaire-9 (PHQ-9).

Results:: (56.7%) were males, (43.3%) were females. (28.8%) were residents, followed by (20.3%) were nurses, (19.7%) were general practitioners, and (16.8%) were specialists. About (44.8%) of the participants were diagnosed with COVID-19 and (75.4%) managed patients with COVID-19. (32%) suffered from moderate difficulty falling asleep, and (30%) have moderate difficulty staying asleep. About (21.2%) said that there sleep problems much interfere with their daily functioning. (34.4%) feel nervous and anxious more than half of the days, while (26%) had the same problem nearly every day. (34.5%) feel tired more than half of the days, while (26%) suffered from the same issue nearly every day.

Conclusions:: The results of this study support the view that poor sleep quality can affect the overall mental health dramatically. Poor sleep quality can cause a psychological problems, such as: depression, and anxiety.
ROLE OF SLEEP DURATION IN THE RELATIONSHIP BETWEEN EDUCATION AND MORTALITY

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\textbf{Background and Aims::} Growing evidence suggests an association between both short and long duration of habitual sleep and adverse health outcomes. In order to determine whether the population longitudinal evidence supports the presence of a relationship between duration of sleep and all-cause mortality, and how education plays a role in mortality outcomes.

\textbf{Methods::} This is a population-based cohort study of the 2005-2010 National Health and Nutrition Examination Survey with mortality data obtained through 2015. Adults aged 20 years or older with sleep duration information were categorized into Low(\leq 6), Medium(7-8), and High(\geq 9) hours. Stratified outcomes of all-cause mortality were evaluated using Cox regression.

\textbf{Results::} Percentage of deaths from low-sleep duration among the population (N=15,586) were higher among individuals without High School (HS) Diploma (12.8\%) versus at least some college education (5.7\%). The mean follow-up was 7.7 years. For all-cause mortality, the overall unadjusted hazard ratio (HR) of individuals without HS Diploma to college-educated individuals was 2.36 (95\% confidence interval [CI], 2.00-2.79, \(p < 0.001\)). Adjusted HR was elevated, 1.59 (CI 1.01-2.52, \(p = .04\)), among those with low-sleep duration but closer to 1.0 (0.89 CI 0.51-1.55, \(p < 0.25\)) among high-sleep duration, after controlling for physical, mental, and demographic risk factors.

\textbf{Conclusions::} Our study shows an unambiguous and consistent pattern of increased risk of dying among individuals with low education. However, this relationship is especially pronounced among individuals who have low sleep duration making it an important determinant of health. Screening for sleep disorders is especially important in the consideration of other neurological disorders.
SLEEP DISRUPTION, AS A CAUSAL AGENT FOR FIBROMYALGIA.

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Background and Aims:: Sleep has an important role in neuronal plasticity and brain cellular signaling and its deprivation can lead different negative effects in brain and cognitive functions. FM is a chronic pain condition with abnormal pain processing and central sensitization. Reports show that sleep deprivation in healthy individuals can induce FM symptoms.

Methods:: A descriptive, cross-sectional study was conducted in 190 FM patients evaluated at the INNAP, Caracas, Venezuela. The ACR criteria for Fibromyalgia, Impact Questionnaire (FIQ), Generalized Pain Index (WPI), Symptom Severity Index (SS), Beck Depression Inventory, State-Trait Anxiety (STAI) were followed. Sleep interruption or fragmentation was evaluated by polysomnography.

Results:: According to the American Academy of Sleep Medicine, we found that all FM patients (48.39 + 13.75 years) had sleep disturbances, 31.38% related to their medical condition, 23.19% moderate to severe apnea, and 45.43% restless legs syndrome. We found a correlation (p = 0.069) between the effectiveness of sleep and the number of awakenings and an association with pain and depression. It is important to note that 100% of FM patients had non-restorative sleep and sleep disturbances as symptoms associated with their FM.

Conclusions:: Our data confirm that sleep disturbances can exacerbate the characteristic symptoms of FM and the importance of the sleep study as a routine diagnosis in patients with FM.
ASSOCIATION OF TRIGLYCERIDE-GLUCOSE INDEX WITH CLINICAL OUTCOMES IN PATIENTS WITH ACUTE ISCHEMIC STROKE RECEIVING INTRAVENOUS THROMBOLYSIS

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Background and Aims:: The Triglyceride-Glucose (TyG) Index is a novel marker of insulin resistance which has been shown to predict poor outcomes in acute coronary syndrome. However, this marker has not been evaluated in acute ischemic stroke (AIS) patients who have received intravenous tissue plasminogen activator (tPA).

Methods:: Consecutive AIS patients who received tPA in a comprehensive stroke centre were studied. TyG Index was calculated using the formula ln[fasting triglycerides(mg/dL) × fasting glucose(mg/dL)/2]. The primary outcome measured was 90-day mortality. Secondary outcomes included early neurological improvement (ENI), poor functional outcome (90-day modified Rankin Scale 3-6) and symptomatic intracranial hemorrhage (SICH). Adjusted logistic regression evaluated associations of TyG index with outcomes.

Results::
Of 698 AIS patients, TyG index was significantly lower in patients that survived at 90-days than those who died (8.61 [IQR: 8.27-8.99] vs 8.76 [IQR: 8.39-9.40], p=0.007). After adjustment for hypertension, age, NIHSS and presence of large vessel occlusion (LVO), TyG index remained significantly associated with 90-day mortality (adjOR: 1.97, 95% CI:1.34–2.90, p<0.001). Lower TyG index was found among those who achieved ENI (8.56 [IQR: 8.26-8.92] vs 8.69 [IQR: 8.31-9.08], p=0.006). On ordinal shift analysis, having 'high TyG' (TyG Index ≥ 9.28) was associated with an unfavorable shift in mRS outcomes (adjOR: 2.45, 95% CI: 1.67–3.60, p<0.001).

**Conclusions:** In AIS patients who received tPA, a higher TyG index or degree of insulin resistance was significantly associated with increased 90-day mortality and poorer outcomes.
ENDOTHELIAL NITRIC OXIDE SYNTHASE (GLU298ASP) POLYMORPHISM IS ASSOCIATED SIGNIFICANTLY WITH ISCHEMIC STROKE PRESENTING WITH SEIZURES AND ALTERED SENSORIUM

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Background and Aims:: Endothelial nitric oxide synthase (eNOS) is an enzymatic marker whose genetic polymorphism might predispose to acute ischemic stroke (AIS) via vascular endothelial dysfunction. It has potential role in atherosclerosis, making it a plausible risk factor for stroke. Prior studies have failed to prove a conclusive relationship between eNOS polymorphism and AIS. The aim of this study is to find an association between the presence of eNOS polymorphism (Glu298Asp) and the risk of developing AIS.

Methods:: Materials and Methods: We recruited 307 subjects including 153 AIS cases and 154 healthy controls. The eNOS (Glu298Asp) polymorphism was identified in EDTA blood by PCR amplification of the target region followed by restriction enzyme digestion, and genotyping on Agarose gel. GG, GT and TT genotypes were obtained. Statistical analysis was done using SPSS software version 20.

Results:: A significant association was found between the presence of TT genotype and the risk of AIS (Odd’s ratio (OR): 2.43, P-value = 0.038). There was no significant association between the TT genotype and the traditional stroke risk factors. However, the TT genotype was significantly associated with the presence of altered consciousness (OR: 5.27, 95% CI: 1.59–17.04, P-value = 0.003) and with the occurrence of seizures at presentation (OR: 7.98, 95% CI: 1.99–32.09, P-value = 0.007).

Conclusions:: There is a significant association between the presence of eNOS polymorphism (Glu298Asp) and the risk of AIS, and the TT genotype may predispose to a more severe initial presentation of ischemic stroke.
ROLE OF ACE POLYMORPHISM IN ACUTE ISCHEMIC STROKE

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Background and Aims:: Stroke is one of the leading causes of death and disability in India. Angiotensin-converting enzyme (ACE) is involved in the development of hypertension, atherosclerosis, cardio, and cerebrovascular disease and is a plausible genetic candidate for stroke. The role of ACE polymorphism is still uncertain and requires further investigation. The aim of this study was to study the role of ACE insertion/deletion polymorphism in acute ischemic stroke (AIS).

Methods:: Materials and Methods: One hundred thirty AIS cases and 130 age and sex matched healthy controls were recruited. Ten milliliters venous blood was drawn and 6 mL of blood was used for routine hematological, biochemical tests. Remaining 4 mL of EDTA blood was used for DNA extraction, PCR amplification, and restriction digestion. Three genotypes (II, ID, and DD) were visualized on 3% agarose gel. Association between genotypes among stroke case was done by Chi-square test with P-value <0.05 taken as significant.

Results:: DD genotype was significantly associated with the risk of stroke with P-value of 0.0001. Both the dominant and recessive models showed that the DD genotype was independently associated with an increased risk of ischemic stroke (OR= 20.732; 95% CI: 2.7241–157.7864; P-value= 0.003 for the recessive model and OR= 2.848; 95% CI: 1.5127–5.3649; P-value= 0.001 for dominant model).

Conclusions:: Our study showed a strong association between ACE polymorphism and the risk of AIS. This study paves the way for further studies to confirm the role of ACE polymorphism as genetic risk factors for AIS.
MASSIVE HEMORRHAGIC TRANSFORMATION IN PATIENT PREVIOUSLY TREATED WITH TICAGRELOR WITH ACUTE ISCHEMIC STROKE TREATED WITH ALTEPLASE

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Background and Aims:: Patients with acute ischemic stroke treated with intravenous thrombolysis are often under previous treatment with antiplatelet drugs. The safety of Ticagrelor in this clinical scenario is unknown.

Methods:: We present a case report of a patient attended, admitted and treated in Neurology and Critical Care Unit of our hospital.

Results:: 88 year old male, previously under treatment with Acetylsalicylic Acid (100 mg) and Ticagrelor (90 mg) as dual antiplatelet therapy following acute myocardial infarction five months before, was admitted to the emergency room with acute hemiparesis and aphasia. The diagnosis was acute ischemic stroke (NIHSS 7) and the patient was treated with intravenous thrombolysis with Alteplase 90 minutes after the onset of symptoms. Despite being transferred to the Intensive Care Unit and being under treatment with Labetalol in order to strictly control blood pressure, the patient's condition worsened in the following days and a massive intracranial hemorrhagic transformation was found. A comfort care based approach was adopted and the patient died within the next 3 days.

Conclusions:: Antiplatelet therapy is widely used in patients with minor stroke, but Ticagrelor is currently not recommended for stroke or high risk transient ischemic stroke prevention. The evidence about safety of Ticagrelor pretreatment in patients suffering from acute ischemic stroke treated with intravenous thrombolysis is scarce, and further studies must be performed to determine the safety of Ticagrelor in this particular clinical scenario.
NEUTROPHIL TO LYMPHOCYTE RATIO AS A PREDICTOR OF ATRIAL FIBRILLATION IN ISCHEMIC STROKE

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Background and Aims:: Neuroinflammation is one of the main determinants of the final damage in ischemic stroke. Neutrophil to Lymphocyte Ratio (NLR) is a systemic inflammation biomarker, which has been related to poor outcome in ischemic stroke and to a higher risk of Atrial Fibrillation (AF). However, little is known about the association between NLR and AF in ischemic stroke patients.

Methods:: We enrolled patients admitted for acute ischemic stroke to the Stroke Unit of the Ospedali Riuniti Ancona from January 2019 to December 2019. For each patient we collected sex, age, stroke’s features, white blood cells count and subtypes on admission. We evaluated the occurrence of new-onset AF, the presence of pre-existing AF and the presence of any type of AF.

Results:: We evaluated 153 subjects (mean age 70,7 ± 11,8 years; 53% males) of whom 23 (15,0%) had pre-existing AF and 21 (13,7%) had new-onset AF. Patients affected by any form of AF had a significantly higher NLR than patients without AF (p=0,001). Patients with new-onset AF had a mean NLR of 8,0 ± 7,1, significantly higher than the cohort without, which was 4,7 ± 4,1 (p=0,003).

Figure 1: Neutrophil to Lymphocyte ratio (NLR) differences between patients with Atrial Fibrillation (AF) and patients without AF
Conclusions:: Inflammation plays a key role on AF development and maintenance. Therefore, NLR could reflect a higher systemic inflammation which can favor AF insurgence. Future larger studies are needed to clarify the relationship between AF and NLR as a biomarker of suspected cardioembolic stroke.

Figure 2: Neutrophil to Lymphocyte ratio (NLR) differences between patients with new-onset Atrial Fibrillation (AF) and patients without new-onset AF.
AMAUROSIS FUGAX DUE TO RADIATION INDUCED CAROTID STENOSIS TREATED BY CAROTID ARTERY STENTING

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Background and Aims:: Amaurosis fugax can be a presentation of a patient presenting with radiation induced carotid artery stenosis and such patients can be safely managed by carotid angioplasty and stenting.

Methods:: A 59 year old male, presented with four episodes of transient, painless loss of vision in the right eye since past 20 days which resolved spontaneously and completely. The patient had a history of oropharyngeal squamous cell carcinoma three years ago, for which he had received 6 cycles chemotherapy along with radiotherapy. MRI brain with angiogram was suggestive of diffuse long segment wall thickening with luminal narrowing of Right Internal Carotid Artery without any acute infarct or hemorrhage; which was confirmed by 4 vessel digital subtraction angiogram.

Results:: He underwent Right Carotid Artery angioplasty using a cutting balloon using a distal protection device, followed by stenting. Patient had no further episodes and did well on follow-up.

Conclusions:: Thus, amaurosis fugax can be a presentation of a patient with carotid artery stenosis after radiotherapy and such patients can be safely managed by carotid angioplasty and stenting.
UNUSUAL CAUSE OF STROKE IN YOUNG, A CASE OF BOW HUNTER SYNDROME

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Background and Aims:: Bow hunter's syndrome is a rare vascular phenomenon characterized by dynamic insufficiency of the posterior cerebral circulation induced by rotation of the head within normal physiologic range and may lead to transient ischemic symptoms.

Methods:: We report a case of an 18-year-old male with vertebro-basilar stroke. On dynamic imaging with neck rotated to right, there was complete cessation of flow through left vertebral artery which was suggestive of Bow hunter syndrome. The right vertebral artery was normal even after dynamic imaging. There was a single PICA originating from the left vertebral artery that was supplying both the sides. There was a dysplastic left arch of atlas and bony spur and c7 vertebral anomaly with single posterior inferior cerebellar artery.

Results:: In view of the single stroke episode, patient was advised conservative management on antiplatelets, cervical collar and was advised to avoid turning neck to the right. On follow up after 3 months, he had no further such episodes.

Conclusions:: In this case, the most likely cause was significant narrowing of left foramen transversarium at C7 vertebra and the cause of vertebral artery dissection was the small superior bony projection at left arch of atlas. It is a rare presentation of congenital cranio vertebral junction anomaly with vertebro-basilar insufficiency. In regards to our patient, since symptoms were mild, conservative treatment and continued stroke prophylaxis by antiplatelets was pursued at this time with no surgical intervention.
INTRAVENOUS ADMINISTRATION OF DANTROLENE AND NIMODIPINE IN COMBINATION SIGNIFICANTLY IMPROVES CEREBRAL BLOOD FLOW PERFUSION IN A RAT MODEL OF CEREBRAL-INDUCED VASOSPASM

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Background and Aims:: Experimental evidence shows that concomitant administration of dantrolene and nimodipine has synergistic effects in reducing vasospasms in aortic rings from Sprague Dawley rats. To determine if this effect extends to the cerebral circulation, we investigated the effect of intravenous administration of dantrolene (2.5 mg/kg) and nimodipine (1 mg/kg and 2 mg/kg) on MCA blood flow velocity (BFV) in Sprague Dawley rats.

Methods:: BFV was evaluated with a Laser Doppler System seven days after induction of cerebral vasospasms. Mean blood pressure (MBP) and heart rate (HR) were also measured.

Results:: Individual administration of these drugs resulted in similar reductions in BFV (34% with dantrolene, n=6, p<0.05; 32% with nimodipine 2 mg/kg, n=6, p<0.05). Moreover, dantrolene combined with 1mg/kg of nimodipine decreased BFV by 48% (from 435.70 ± 21.50 to 284.30 ± 26.10 perfusion units, n=6, p<0.05). Similarly, dantrolene combined with 2 mg/kg of nimodipine, reduced BFV by 54% (from 536.00 ± 32.60 to 367.80 ± 40.90 perfusion units, n=6, p<0.05).

Conclusions:: The combination of dantrolene and 1mg/kg of nimodipine, did not alter MBP or HR. Thus, concurrent administration of 2.5 mg/kg dantrolene and 1 mg/kg nimodipine significantly reduces BFV in the MCA without altering hemodynamic parameters. Therefore, adding dantrolene to current standard pharmacological therapies may allow a dosage reduction of CCB and minimize the systemic secondary effects of these drugs. Furthermore, if our findings with rats are applicable to humans, the combined use of dantrolene and nimodipine at optimal doses may be effective in reducing CVSPs. Supported by NIH-MBRS-RISE Grant R25GM061838, and NIMHD-CCRHD-RCMI (U54-MD007600).
FUNCTIONAL OUTCOME AFTER RECANALIZATION THERAPY FOR BASILAR ARTERY OCCLUSION: A SINGLE CENTER EXPERIENCE

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Background and Aims: Acute ischemic stroke due to basilar artery occlusion (BAO) is a life-threatening condition with a mortality up to 90% if left untreated. The current practice of recanalization therapy consists of pharmacological thrombolysis and endovascular mechanical thrombectomy. This study aimed to determine predictors of functional outcome in those patients.

Methods: We conducted a retrospective data analysis of 57 patients with verified BAO in whom recanalization therapy was performed in the period from February 2016 to October 2019. Good functional outcome was defined as mRS 0-2, while successful recanalization as mTICI 2b-3. Futile recanalization was defined as mRS 6 despite successful recanalization.

Results: Mechanical thrombectomy was performed in 53 out of 57 (93%) patients included in our study preceded by intravenous thrombolysis in 21 (36.8%) patients. Successful recanalization was achieved in 64.9% (n= 37) of cases. Overall, 28.1% (n= 16) of patients achieved good functional outcome. Mortality was 52.6% (n= 30). In a multivariate analysis, atrial fibrilation was shown to be a statistically significant predictor of mortality in patients (p= 0.016), but also a significant predictor for futile recanalization (p=0.040) which occured in 35.1% of patients. Initial NIHSS was the only statistically significant predictor of good functional outcome (p= 0.006).

Conclusions: This study suggested that functional outcome after recanalization therapy for BAO may be influenced by the initial stroke severity and the presence of atrial fibrilation. Futile recanalization might be the reason for unfavourable functional outcome in patients with successful recanalization.
Background and Aims:: Anatomical cerebral arteries variations are relatively common. Their knowledge has become essential with the development of stroke treatments.

Methods:: Case report.

Results:: A 70-year-old man with a history of hypertension, smoking, and diabetes was found comatose. Brain CT was normal. CT-angiography showed an ulcerated atherosclerotic plaque in the right internal carotid artery (ICA, panel A) and full fetal origin of the right-sided posterior cerebral artery (PCA, panel B; panel C: schematic representation of the intracranial circulation). Brain MRI demonstrated bilateral thalamic infarction (right>left) consistent with acute ischemic stroke (panel D-F). Echocardiography and prolonged EKG monitoring resulted normal. The patient was diagnosed with artery of Percheron (AOP) territory stroke, likely due to artery-to-artery embolism originating from the right ICA.

Conclusions:: When PCA arises directly from the ipsilateral ICA, it’s defined “fetal”. AOP is a rare anatomical variant consisting of a single perforating artery arising from one of the PCAs and supplying both thalami. The diagnosis of an occluded AOP is inferred from the peculiar ischemic pattern, since AOP cannot be displayed by conventional angiography. In most cases, thalamic involvement is asymmetrical being greater on the side of AOP origin. Signs and symptoms include decrease consciousness, memory deficit, impaired eye movements. Given the lack of “classic” stroke signs, the majority of these strokes go overlooked in the emergency setting leading to delay of time-sensitive treatments. Keeping AOP infarcts
in the differential diagnosis of stupor and coma, and being aware of vascular variations, is critical to avoid misdiagnosis of potentially treatable syndromes.
CLEVELAND CLINIC ABU DHABI: STROKE PATIENTS JOURNEY FROM REFERRING HOSPITAL TO DISCHARGE, METHODOLOGY

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Background and Aims:: Healthcare organizations in the United Arab Emirates (UAE), are looking for ways to improve the quality of services and to increase productivity. In the UAE stroke patients receive healthcare services from acute hospitals, dedicated stroke centers, rehabilitation and home care facilities. Cleveland Clinic Abu Dhabi (CCAD) is a stroke referral centre that operates as a 24/7 comprehensive neurovascular service providing thrombolysis and thrombectomy. Objectives: We aimed to map the journey of the stroke patients admitted to CCAD from the referring provider to post-acute care.

Methods:: Data was collected from March 2015 till the end of February 2019. The patients' pathways were mapped for both origins of admission to CCAD and discharge destination. We assessed patients' demographics, details of stroke and treatment, and health outcomes. The mapping was constructed using Bayesian Network analyses.

Results:: 1,550 patients (Mean age= 56 +/-15.76 years, Male (67%)) were tracked from five distinct routes: home (57%), CCAD (0.6%), other public/private hospitals or rehabilitation stroke centres (42%), and overseas point of entry; the final overlapping pathways account for 97.5% of the patients. These are direct local home discharges (72%), local rehabilitation centers (5%), local inpatient transfers (5%), deceased (6.5%), or repatriated to their home countries (9.5%).

Conclusions:: This study delineates the journeys of stroke patients receiving stroke services in the emirate of Abu Dhabi through the CCAD’s system. Mapping the journey of these patients advances our understanding of their interactions with other local healthcare organizations, and allows us to determine areas for service development at the country level.
A CASE SERIES: ARTERY OF PERCHERON SYNDROME

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Background and Aims:: Thalamus and midbrain share a complex blood supply from perforators arising from posterior cerebral artery (PCA) and posterior communicating artery. Artery of Percheron (AOP) is a rare anatomic variant arising from a PCA supplying paramedian thalami bilaterally and rostral midbrain. Occlusion of AOP infarcts with characteristic symptoms of vertical gaze palsy, memory impairment and coma called AOP Syndrome. It accounts for 0.3% of ischemic strokes. We share experience of managing four case of AOP strokes.
Methods:: All four of our patients presented with sudden collapse followed by loss of consciousness or fluctuating conscious level. Encephalitis and seizure were suspected and treated accordingly. Speech was dysarthric and cranial nerve abnormalities i.e. oculomotor and facial nerve palsy were noted. Patients had no recall of their presentation. Standard management was done in Hyperacute Stroke Unit. One of the patients received IV thrombolysis therapy. Another patient was complicated by pneumonia and pulmonary embolism (PE) and was treated with antibiotics and anticoagulation. Complete stroke diagnostic workup was requested. Initial CT head was unremarkable in all. Subsequently, MRI Brain showed acute bithalamic infarcts.
Unfortunately, the patient who had chest infection and PE succumbed to death. However, other three patients were discharged home after inpatient MDT rehabilitation with minor residual neurology.

**Conclusions:** Occlusion of AOP causes a rare ischemic infarct syndrome. Symptom complex of AOP syndrome may vary according to location of stroke. Having a Low threshold for clinical suspicion of AOP involvement makes early diagnosis possible. Prompt diagnosis allows earlier initiation of standard treatment. This has positive effects on prognosis.
THE ROLE OF PLATELET AGGREGATION IN HYPERTENSIVE INTRACEREBRAL HEMORRHAGE

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Background and Aims:: Small penetrating vessels are a major source of bleeding in acute hypertensive intracerebral hemorrhage (ICH). The goal of this study was to evaluate the role of platelet aggregation in hematoma formation and evolution.

Methods:: Fifty patients with acute hypertensive ICH were included in the study. At admission, platelet aggregation tests were performed using a Biola LA230-2 aggregometer. Adenosine diphosphate, collagen, ristocetin, epinephrine, and arachidonic acid were used as aggregation inducers. A baseline computed tomography was obtained in every case. A partial least squares structural equation model was constructed in order to evaluate the relationship between platelet aggregation and intracerebral hemorrhage. The study was approved by the Local Ethics Committee.

Results:: A "Platelet Aggregation" latent variable (composite reliability = 0.719) was inferred from aggregate sizes measured during induced platelet aggregation tests with all inducers. A "Hematoma" latent variable (composite reliability = 0.811) was inferred from hematoma volume, midline shift, and the presence of an intraventricular extension of hemorrhage at admission. The total effect of the "Platelet Aggregation" latent variable on the "Hematoma" latent variable was -0.410 [95% CI from -0.665 to -0.296, T = 2.716, p = 0.007], indicating that low platelet aggregation was a poor prognostic factor in acute hypertensive ICH.
Conclusions: Platelet aggregation plays a major role in hematoma formation and evolution in acute intracerebral hemorrhage.
INTERLEUKIN-6 AND INTERLEUKIN-8 CONCENTRATIONS ARE PREDICTORS OF POOR OUTCOME IN ACUTE HYPERTENSIVE INTRACEREBRAL HEMORRHAGE

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Background and Aims:: Interleukin-6 (IL-6) and interleukin-8 (IL-8), produced by macrophages, are major inflammatory cytokines. It is known that M1 macrophage activity (indicated by IL-6 upregulation) plays a major role in ischemic stroke. However, this subject is less studied in intracerebral hemorrhage (ICH). The goal of this pilot study was to investigate the role of IL-6, IL-8, and M1 macrophage activity in acute hypertensive ICH.

Methods:: In 24 acute ICH patients, blood plasma samples were collected and stored at minus 80 degrees Celsius. IL-6 and IL-8 concentration analysis was performed using a multiplex immunoassay. 21-day MRS score was obtained from medical records. The study was approved by the Local Ethics Committee.

Results:: There was a strong positive correlation between IL-6 and IL-8 concentrations ($r_s = 0.651, p = 0.001$) indicative of macrophage transition to M1 phenotype. In univariate models, IL-6 and IL-8 concentrations were predictive of in-hospital death [OR = 1.088 per 1 pg/mL of IL-6, 95% CI 1.009 - 1.174, $p = 0.029$ and OR = 1.124 per 10 pg/mL of IL-8, 95% CI 1.004 - 1.260, $p = 0.043$]. Additionally, in univariate models, IL-6 and IL-8 concentrations were predictive of higher 21-day MRS score [OR = 1.138 per 1 pg/mL of IL-6, 95% CI 1.063 - 1.263, $p = 0.002$ and OR = 3.646 per 10 pg/mL of IL-8, 95% CI 1.840 - 8.930, $p = 0.001$].

Conclusions:: A combination of IL-6 and IL-8 is an important marker of M1 macrophage activity in ICH and a predictor of 21-day disability and in-hospital death.
ROLE OF SOCIO-ECONOMIC STATUS IN CHOOSING THROMBOLYTIC AGENT AND ITS OUTCOME IN ACUTE ISCHEMIC STROKE: DATA FROM A TERTIARY CARE CENTER IN NORTH INDIA

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Background and Aims:: Alteplase, a recombinant tissue-type plasminogen activator(rtPA) is the only FDA-approved thrombolytic drug in acute ischemic stroke(AIS). Tenecteplase is a modified rtPA which is cheaper. Cost is a major concern in stroke thrombolysis. We aimed to study role of Socio-economic status(SES) in patients' preference of thrombolytic agent and its outcome.

Methods:: This prospective observational study conducted in PGIMER, a tertiary care center in India, recruited AIS patients thrombolysed between July 2017 and September 2018. We studied variables including SES based on modified Kuppuswamy scale, thrombolytic agent chosen and outcome in terms of modified Rankin Scale(mRS) after 3months.

Results:: 39 patients received tenecteplase and 39 patients received alteplase. 7 patients belonged to upper class, all of whom(100%) chose alteplase. 30 patients belonged to upper middle class, of whom 25(83.3%) and 5(16.7%) patients chose alteplase and tenecteplase respectively. 25 patients belonged to lower middle class in which 7(28%) and 15(72%) chose alteplase and tenecteplase respectively. 20 patients were in upper lower class, of whom 4(20%) and 16(80%) chose alteplase and tenecteplase respectively. The between group difference in distribution of SES in tenecteplase and alteplase groups was statistically significant(p=0.000). Median mRS scores at 3months were 3.5 and 3 in tenecteplase and alteplase groups respectively, the difference being statistically insignificant(p=0.608). There was no correlation between SES and 3month-mRS score in tenecteplase (Spearman’s rho= 0.101, p=0.398) and alteplase groups (Spearman’s rho= -0.035, p=0.834).

Conclusions:: Majority of patients in upper and lower SES chose alteplase and tenecteplase respectively. However, there was no correlation between outcome and SES in both the groups.
FREQUENCY OF CEREBRAL INFARCTION AND INTRA-EXTRACRANIAL ARTERY STENOSIS IN MONGOLIAN YOUNG ADULTS

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Background and Aims: The frequency of cerebral infarction and stenosis of intra- and extracranial arteries may vary with age-group and gender. This study was conducted to clarify the risk factors and characteristics of cerebral infarction and stenosis of vessels in Mongolian young adults.

Methods: This was a prospective study, from October 2015 to July 2020, of 100 patients below 50 years diagnosed with acute cerebral infarction. Patient characteristics were compared according to sex (61 males and 39 females) and age group (29 patients were below 34 years and 71 patients were 35–49 years). Characteristics of acute cerebral infarction were studied by DWI-diffusion weighted MRI imaging. Stenosis of intra- and extracranial arteries was diagnosed by duplex sonography, head and cervical magnetic resonance angiography (MRA).

Results: Leading causes for cerebral infarction in the young patients were hypertension (71%), smoking (57%), dyslipidemia (45%), diabetes (33%), and migraine with aura (25%). Lacunar Infarction was most common in our patients (33%). Partial anterior circulation infarction was predominant in males (45.9% vs 38.5%; P < 0.05) and posterior circulation infarction in females (23.1% vs 11.5%; P < 0.05). Small artery atherosclerosis was found in 33% of cases, with higher prevalence in patients of the 35–50 years age-group. Intracranial stenosis was more common than extracranial stenosis, and middle cerebral artery stenosis was most prevalent (38.9%). Stenosis in the anterior circulation was more frequent than in the posterior circulation (P < 0.001).

Conclusions: In these young patients, hypertension, smoking, dyslipidemia, diabetes, and migraine with aura were common risk factors. Intracranial stenosis was most common, particularly in the middle cerebral artery.
PREVALENCE AND PATTERN OF ADVERSE EVENTS IN PATIENTS RECEIVING INTRAVENOUS THROMBOLYSIS FOR ACUTE ISCHAEMIC STROKE

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Background and Aims:: BACKGROUND Thrombolysis should be offered to all patients with Ischemic stroke who meets the selection criteria. It involves the intravenous infusion of tissue plasminogen activator tPA, which in our Trust is Alteplase. The rationale is to break down the clot in the blood vessel and restore blood flow to save the area of penumbra
AIMS •To determine the prevalence of adverse events •To highlight the different types of adverse events •To find out if there is aggregation of these adverse events to certain period of the day or months

Methods:: •This was a retrospective and prospective audit spanning between January and December 2020. The data was obtained from SSNAP and patients record, study conducted in the Acute Stroke Unit of Worcester Royal Hospita, United Kingdom All patients with acute Ischemic stroke who received thrombolysis were included in the study

Results:: •A sizeable numbers of patients who were administered Intravenous thrombolysis 42% developed various types of adverse reactions. •Bleeding complication both intracerebral and extracranial were the commonest encountered adverse events making up 46% •Out of hour thrombolysis resulted in more proportion of adverse events 46% as compared to 37% during normal working hours.

Conclusions:: •The NICE and RCP guidelines emphasizes offering thrombolysis to all patient with acute ischemic stoke who meets the selection criteria. •The percentage of compliance of 12.7% thrombolysis in this audit though similar to the national average is an indication that many factors are responsible for the relatively low level of thrombolysis in ischemic stoke.
Background and Aims:: Cervical artery dissections (CAD) are responsible for 10-25% of stroke in young adults, prior mild trauma is identified in up to 40% of cases. However, triggering or risk factors are absent in many patients so we should always include CAD in the etiological study of undetermined stroke.

Methods:: We present a case of CAD with recurrent stroke and difficult diagnosis due to its atypical presentation.

Results:: A 36 year old healthy man is brought to the emergency room after a mild car accident caused by sudden onset blurry vision and dizziness while driving. The previous days he had experienced spontaneous self-limited cervical pain and vomits. Physical examination reveals bradypsychia without focal neurological deficits. Urgent computed tomography (CT) scan shows capsulothalamic hypodensity suggestive of previous stroke. Rapidly onset dysphagia, dysarthria and dyspnea appear the following day; vocal cord paralysis is detected and the patient is intubated. After cerebrospinal fluid (CSF) analysis reveals 15 leukocytes, and given epidemiological context of gastroenteritis, Lysteria monocytogenes rhomboencephalitis is suspected. However, after 24 hours of antiobiotherapy, CSF is normalized and magnetic resonance (MRI) shows lesions compatible with cerebellar, hemimedullary and capsulothalamic infarction as well as right vertebral threadlike flow suggestive of dissection. The patient starts anticoagulation therapy and evolves favourably without recurrences.
Conclusions:: Diagnosis of CAD is made by angio-CT or angio-MRI; arteriography is limited to cases with high level of suspicion despite normal non-invasive neuroimaging. As for treatment, antiplatelet therapy is preferred in intracranial CAD; in extracranial CAD anticoagulation and antiplatelet therapy are both equally effective and safe.
THE INVOLVEMENT OF THE FACTOR V G1691A GENE ON RECURRENT ISCHEMIC STROKE IN YOUNG ADULTS

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Background and Aims:: Although the association between traditional risk factors and ischemic stroke (IS) recurrence has been widely studied, the involvement of inherited thrombophilia such as the factor V G1691A gene (FV) in stroke recurrence has not been clearly defined. This study aims to determine the involvement of the FV in recurrent ischemic stroke in young Tunisians.

Methods:: We included retrospectively all young adults of age 18–50 years with first-ever ischemic stroke who were treated in the neurology department during a period of 5 years. The predictive effect of all demographic characteristics, traditional risk factors and clinical data were collected, a complete etiological assessment, and genetic test was screened.

Results:: The diagnosis of ischemic stroke was confirmed in 200 patients. Among them, 93 had a second stroke within two years following the first attack. The heterozygous form of FV polymorphism present in 32 patients, 66% for the recurrent stroke population. Statistical analysis found a significant association between recurrent stroke and heterozygous factor V variant (p: 0.018).

Conclusions:: The study emphasizes the important role of factor V G1691A genetic screening in patients with stroke in this region. In order, to optimize secondary prevention of stroke to keep safe lifetime events, to improve survival, and to have more successful aging.
TWO CASES OF WATERSHED-PATTERN REVERSIBLE ENCEPHALOPATHY SYNDROME

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Background and Aims:: Posterior reversible encephalopathy syndrome (PRES) is a clinicoradiological syndrome characterized by several features, including headache, impaired consciousness, visual disturbances, seizures and vasogenic edema on brain MRI scans. Despite the typical parietal and occipital lobe localization, many reports showed involvement of other brain areas. We describe two cases of reversible encephalopathy syndrome involving brain watershed zones.

Methods:: Two women (51 y.o. and 77 y.o.) were admitted to our Neurology Department; the first patient was admitted for confusion, gait ataxia, speech and visual disturbances occurred after abdominal pain, vomiting and fever; the second one came to our hospital for impaired awareness with right upper limb clonic movements, after recurrent vomiting with severe hypomagnesemia. Both patients showed high blood pressure values. In both cases the Brain MRI showed FLAIR DWI signal abnormalities with a bilateral watershed distribution. The management of blood pressure and metabolic disorders in these patients led to clinical remission of symptoms.

Results:: Considering the clinicoradiological features, a diagnosis of reversible encephalopathy syndrome was made.

Conclusions:: PRES may be caused by the loss of vascular autoregulation with blood-brain barrier disruption and vasogenic edema which might be triggered by increased systolic blood pressure or endothelial dysfunction. Since there are no specific diagnostic criteria for PRES and considering the role of brain MRI in the diagnosis, the knowledge of imaging patterns other than the original parieto-occipital ones (including hemispheric watershed distribution), along with the evaluation of suggestive neurological features in appropriate clinical settings could help the neurologist to a correct diagnosis and management.
HYPERHOMOCYSTEINEMIA FOLATE AND VITAMIN B12 IN YOUNG ISCHEMIC STROKE

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Background and Aims:: Hyperhomocysteinemia (Hhcy) is associated with cerebrovascular disease, including ischemic stroke. Homocysteine level is influenced by folate and vitamin B 12 (VB 12), the substrate and cofactor of its metabolism.

Methods:: This is a cross-sectional study of patients under 50 years of age followed for stroke over a 2-year period. All patients received a comprehensive etiologic evaluation that included cardiac and arterial vascular axis assessment. an assay Hcys, folate and VB12 was performed.

Results:: We collected 109 patients with a mean age of 39.6± 6.5 years and a sex ratio of 1. A rise in homocysteine levels was noted in 46.6% of cases (18.8 ± 7.5 µmol/l; p≥ 0.05). In fact, 50 patients had a folate deficiency (2.08 ± 0.7 µmol/l; p≥ 0.05), 16 cases had a VB 12 deficiency (189.5 ± 232.2; p:0.52). A significant correlation between folate deficiency and moderate homocysteine level (21.1± 9.2; p:0.03).

Conclusions:: Hhcy appears to play a role in the genesis of stroke, is mainly associated with a decrease in folate, systematic testing in patients with ischemic stroke would be important for the eventual administration of vitamin therapy.
A RARE CASE OF A NINE SYNDROME WITH A DWI-NEGATIVE IMAGING IN A FILIPINO ADULT

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Background and Aims:: The brainstem contains important structures that give an array of clinical manifestations in pathologic process. Here, we report a case of “Nine Syndrome” in an adult Filipino male with no acute findings on DWI imaging. The exact prevalence of Nine Syndrome has been accounted to only less than ten cases reported in the literature noted to be due to a pontine tegmentum lesion.

Methods:: A Case Report

Results:: This is a case of a sixty-five year old male, who had a five-hour history of sudden onset of dizziness. Pertinent neurologic findings revealed an exotropic left eye confirmed by an assymetrical Hirschberg test, with no adduction and corrective saccades upon abduction, with frozen horizontal gaze; right-sided peripheral facial palsy and left-sided weakness of 4/5 and sensory loss of 30%. Using a 1.5T MR cranial scanner with time-of-flight (MRA), there was no evidence of acute territorial infarct but an old lacunar infarct in the right pontine tegmentum with normal course and caliber of both the anterior and posterior circulations. Patient was started on dual anti-platelet, high dose statin, and started on anti-hypertensives on the fourth hospital day. He was then sent home improved.

Conclusions:: Nine syndrome is a rare case and this is the first case of Nine Syndrome in a Filipino patient based on literature. Its diagnosis rely on its clinical manifestations, neuroanatomy, and imaging that may yield a negative finding. This should not impede the clinicians in its early recognition and management.
EMERGENCY STROKE MANAGEMENT DURING COVID-19 PANDEMIC: EXPERIENCE FROM TRIVENETO AREA

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Background and Aims:: COVID-19 pandemic is a major problem for global healthcare. There are many challenges for stroke emergency chain to maintain high medical care levels: many European Countries showed changes in neurological admissions and treatments. Our aim was to investigate the amount of admissions and treatment of stroke patients Friuli-Venezia-Giulia, Veneto and Trentino-Alto-Adige during the first wave of COVID-19.

Methods:: We retrospectively collected patients admitted to most Triveneto Stroke Units, eventually treated with thrombolysis or thrombectomy, from January to May 2020 (the first Italian pandemic wave). Primary endpoint was the number of patients arriving to these Stroke Units; secondary endpoints were number of thrombolysis and/or thrombectomies. Chi-square analysis was used on all patients; furthermore patients were divided into two cohorts (pre-lockdown and lockdown) and Kruskal-Wallis test was used.

Results:: 2536 patients were admitted in 22 centres. There was a significant decrease (p=0.016) of admissions in April (464) compared to January (570); significant decrease (p=0.032) of thrombectomies in April (32) compared to January (64); thrombolysis rate was unaffected. Analysing non-COVID-19 period - January and February - and COVID-19 period - March and April - there was a significant decrease of admissions (11%) with a collapse of thrombectomies (42%), while thrombolysis rate remained unchanged.

Conclusions:: We found a decrease of stroke patients admissions in North-East-Italy during first wave period, with no impact on thrombolysis rate, confirming a great response of emergency care system to pandemic; instead the significant decrease in thrombectomy rate addresses some considerations on Triveneto stroke networks organization.
DRAMATIC DECREASE OF STROKE ADMISSIONS DURING THE FIRST WAVE OF COVID PANDEMIC IN ITALIAN-SLOVENIAN CROSS-BORDER AREA: A CLINICAL AND RADIOLOGICAL STUDY

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Background and Aims:: The fear of COVID-19 infection may discourage patients from going to the hospital even in case of sudden onset of disabling symptoms. We aimed to evaluate the effects of the COVID-19 pandemics on stroke management during the first month of Italian lockdown in 2020 in the cross-border Italy-Slovenia area.

Methods:: We analyzed admitted patients' clinical features, outcomes and presenting brain CT perfusion (CTP) patterns between 9th March 2020 and 9th April 2020 (first month of lockdown), and compared them with patients admitted during the same period in 2019.

Results:: Total admissions were reduced by 45% during the lockdown compared to the same period in 2019 (16 vs 29, respectively), and a higher prevalence of severe stroke (NIHSS > 10) on admission (n = 8, 50% vs n = 8, 28%) was noted. During lockdown, worse functional and independence outcomes were found, despite the similar proportion of reperfused patients. Similar 'symptoms alert-to-admission' and 'door-to-treatment' times were observed. Moreover significantly higher total CTP hypoperfused volume (83.3 vs 18.5 ml, p = 0.003), core volume (27.8 vs 1.0 ml, p <0.001), and higher infarct volume on follow-up CT during COVID-19 (35.5 vs 3.0 ml, p < 0.001) vs non-COVID-period was noted.

Conclusions:: During the first wave of COVID-19 pandemic there was a dramatic decrease of stroke admissions in our stroke unit. We noted a higher prevalence of severe stroke with higher NIHSS and CTP core volume, suggesting that minor stroke or TIAs generally preferred to stay home.
Background and Aims:: Although « young ischemic stroke » has been considered a relatively rare event, there is evidence that it is increasing. Despite improvements in diagnosis and treatment, ischemic stroke in young adults can cause a long-lasting disability. There is wanting data regarding young ischemic stroke in developing countries, especially in Tunisia. The purpose of this study was to investigate risk factors and etiologies of young ischemic stroke.

Methods:: A total of 70 young ischemic stroke patients (18-45 years old) were admitted, between 2009 and 2019. Stroke etiologies were classified according the Trial of ORG 10172 in acute stroke treatment (TOAST).

Results:: A total of 70 patients were included, out of which 66% were men. The most frequent traditional risk factors were smoking history (50%), history of high blood pressure (27%), diabetes (24%) and hypercholesterolemia (13%). By TOAST, 37% of patients' stroke etiology was classified as undetermined etiology (TOAST V), 34% as other causes (TOAST IV), 20% as cardioembolic (TOAST II), 6% as large artery atherosclerosis (TOAST I), 3% as small vessel occlusion (TOAST III).

Conclusions:: In our study, traditional risk factors were not-so-uncommon in young adults with ischemic stroke suggesting that prevention can go through controlling these factors. A broad and detailed diagnostic workup is crucial to puzzle out the etiology for more and better stroke prevention.
EMBOLIC STROKES OF UNDETERMINED SOURCE IN YOUNG ADULTS: INCIDENCE, RISK FACTORS AND LONG-TERM OUTCOME

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Background and Aims:: Embolic stroke of undetermined source (ESUS) is a new clinical entity, not yet thoroughly investigated in young stroke patients. In this population-based study, we aimed to compare the clinical characteristics, risk factors as well as outcomes in young adults with ESUS and other aetiological subgroups of strokes.

Methods:: We included 70 patients aged between 18 and 45 years old with first-ever ischemic stroke (IS). Stroke etiologies were classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST), and ESUS patients were identified according to the criteria of Cryptogenic Stroke/ESUS International Working Group.

Results:: Among 70 patients, 19 (27%) were classified as ESUS. They were younger (median age was 35 years vs. 39 Years). Male sex was less common in ESUS (59.2% vs 63.6%). ESUS were of moderate severity (median NIHSS score was 5). They had fewer cardiovascular risk factors than other TOAST groups (less hypertension (24.6% vs. 32.7%, p<0.01), diabetes (16.9% vs. 32.7 ; p<0·01), hypercholesterolaemia (15.3% vs. 25.4% ; p<0-01), and history of smoking (31.5 % vs. 43.2 % ; p=0·01). All patients with ESUS were treated with antiplatelet therapy. A low risk of recurrence stroke was noted in ESUS population (4% vs 13.7%). Patients with ESUS had more favorable functional outcomes.

Conclusions:: In our cohort, ESUS patients were younger and had milder cardiovascular risk factor burden and generally better long-term outcome compared to other causes of young ischemic stroke. Anti-platelet agents remain the first-line treatment for ESUS patients.
MORBIDITY FACTORS OF INTRACEREBRAL HEMORRHAGE

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CHU, Military Hospital Of Tunis, tunis, Tunisia

Background and Aims:: Intracerebral hemorrhage (ICH) is the most disabling and deadly form of stroke. Although morbidities remains high, new data suggest that outcomes can be improved with standardized medical care. The aims of this study is to describe the mobility factors of intracerebral hemorrhage.

Methods:: A retrospective study including 253 patients diagnosed with intracerebral hemorrhage was conducted in the department of neurology of the Military Hospital of Tunis from 2016 to 2020.

Results:: The mean age was 58 years old. By far the most common complication was infectious lung disease (ILD)(39.1%). The mean time to onset of ILD was 5.5 ± 4.6 days with extremes of 1 to 21 days. More than half of the patients (82.9%) with swallowing disorders had developed infectious ILD. Septic shock was the second complication in our series (17.39%) but remains the most serious. Urinary tract infections were noted in 15.8% of cases. Meningitis and thromboembolic complications were more rarely described (8.3% and 12.2%).

Conclusions:: The identification of mobility factors for the ICH makes it possible to optimize the therapeutic procedures and to better organize the care channels.
THROMBOLYSIS IN ACUTE ISCHEMIC STROKE: EXPERIENCE IN TERTIARY CARE CENTER IN DEVELOPING COUNTRY

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Seth GSMC and KEM hospital Mumbai, Neurology, Mumbai, India

Background and Aims:: Stroke is one of the leading cause of death and disability. Rate of IV thrombolysis is much less in India. Stroke units are predominantly available in urban areas that too in private hospitals in India as it’s an expensive treatment. Our hospital caters to lower socio-economic class of patients, so we had to make special provision. We have made drug available free for immediate use & patient has to replace in 48 hrs of thrombolysis. To explore the association between Door to needle time (DTNT) and outcome & assess factors influencing in-hospital delay & DTNT

Methods:: All patients treated with IV tissue plasminogen activator (tPa) between June 2015 and April 2017 were enrolled & studied. Multivariate logistic regression model was used to evaluate outcomes.

Results:: 100 patients were treated with IV tPa within 4.5 hours of symptom onset. 48 had favourable outcome & 6 good outcome (MRS 0-2). 54 had DTNT <60 min. Patients with DTNT <60min significantly associated with post-thrombolysis MRS 0-1 (p<0.005). DTNT significantly affected by time to obtain consent(p<0.005),onset to door time(p<0.005) & NIHSS. Major contribution to in-hospital delay is due to delay in obtaining consent(P<0.005) delay in CT room, while pre-hospital delay was mainly due to unawareness of symptoms.

<table>
<thead>
<tr>
<th>Time interval</th>
<th>Recommended time (min) AHA</th>
<th>Study time (min) Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTPT</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>DTIT</td>
<td>45</td>
<td>60</td>
</tr>
<tr>
<td>DTNT</td>
<td>&lt;60</td>
<td>60</td>
</tr>
</tbody>
</table>

Comparison of DTPT, DTIT, DTNT with AHA guideline
Conclusions: Major hurdle in acute stroke thrombolysis are poor awareness about golden hours of stroke & treatment, delay in reaching to hospital and finance. First two hurdles should be addressed on mass scale to get the impact. To alleviate the financial issue we made drug available for immediate use.

### Comparison of factors causing in-hospital delay with other studies

<table>
<thead>
<tr>
<th>Factors</th>
<th>Our study (%)</th>
<th>Sagar Badachi et al. 2015 (%)</th>
<th>Young Seo Kim et al. 2011 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unawareness about existence of treatment</td>
<td>62.96</td>
<td>98</td>
<td>88</td>
</tr>
<tr>
<td>financial constrain</td>
<td>22.22</td>
<td>56</td>
<td>NA</td>
</tr>
<tr>
<td>No decision making relatives</td>
<td>11.11</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>fear of bleeding</td>
<td>3.70</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

### Patients and Hospital Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All (N=100)</th>
<th>DNT&lt; 60 Min (N=52)</th>
<th>DNT&gt; 60 Min (N=48)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr, mean(SD)</td>
<td>56.25(13.53)</td>
<td>55.12(13.55)</td>
<td>57.53(13.87)</td>
<td>0.622</td>
</tr>
<tr>
<td>NIHSS mean(Rank)</td>
<td>16</td>
<td>26</td>
<td>40</td>
<td>0.00</td>
</tr>
<tr>
<td>Post Tt NIHSS</td>
<td>5.75</td>
<td>3.8(12.60)</td>
<td>7.9(21.53)</td>
<td>0.004</td>
</tr>
<tr>
<td>Onset to door time(mean) (Pre-hospital delay)</td>
<td>113</td>
<td>156</td>
<td>223</td>
<td>0.000</td>
</tr>
<tr>
<td>Post Tt MRS1, no.</td>
<td>48</td>
<td>39</td>
<td>9</td>
<td>0.000</td>
</tr>
<tr>
<td>Post Tt MRS2, no.</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>0.15</td>
</tr>
<tr>
<td>Delay in consent, no.</td>
<td>77</td>
<td>30</td>
<td>47</td>
<td>0.00</td>
</tr>
<tr>
<td>Delay in CT room, no.</td>
<td>57</td>
<td>20</td>
<td>37</td>
<td>0.00</td>
</tr>
<tr>
<td>Complications</td>
<td>7</td>
<td>2</td>
<td>5</td>
<td>0.19</td>
</tr>
</tbody>
</table>
COMPARISON OF FOUR SCORE, GCS AND GCS-P IN PREDICTING OUTCOME AT DISCHARGE IN PATIENTS WITH ACUTE STROKE:

Sadaf Majid¹, Umaira Rafiq¹, Asfandyar Khan Niazi¹, Hina Yusuf¹, Qamar Zaman¹, Maimoona Siddiqui²
¹Shifa International Hospital, Neurology, Islamabad, Pakistan, ²Shifa International Hospital, Shifa Tameer-e-millat university, Neurology, Islamabad, Pakistan

Background and Aims:: Stroke is the second most common cause of death and adult disability. The Glasgow Coma Scale (GCS) is the most commonly used scale, and full Outline of Unresponsiveness (FOUR) score is new validated coma scale as an alternative to GCS. Our aim is to evaluate FOUR scores, GCS-P and GCS in predicting outcomes in patients with acute stroke.

Methods:: We prospectively studied consecutive adult patients with acute ischemic and hemorrhagic stroke (less than 48 h after onset) admitted to our stroke unit. FOUR scores, GCS, GCS-P and demographic profiles were documented at admission and discharge.

Results:: We included 120 patients with a mean age of 61.87±14.46. Most of the participants were males 68 (56.7%). Diabetes was seen in 57 (47.5%) patients, hypertension in 86 (71.7%), ischemic heart disease in 22 (18.3%), end stage renal disease in 7 (5.8%), and atrial fibrillation in 8 (6.7%) patients. Mean GCS was 12.32± 2.86, mean GCS-P was 12.13±2.95 and mean mRS at 3 months was 3.18±1.59. There was a significant correlation between mRS at 3 months and GCS (correlation coefficient -.46; p value <0.01), GCS-P (correlation coefficient -.45; p value <0.01) and FOUR scores (correlation coefficient -.56; p value <0.01).

Conclusions:: Our study showed that mRS at 3 months after stroke significantly correlated with GCS, GCS-P and FOUR scores. However, the strongest correlation was with FOUR scores followed by GCS. GCS-P, on the other hand, did not have a stronger correlation with mRS than GCS.
Background and Aims:: Stroke is a leading cause of death worldwide consisting mostly of ischemic strokes, which are most effectively treated with thrombolysis. A high neutrophil to lymphocyte ratio (NLR) is associated with poor functional outcome at 3 months, higher mortality and a higher hemorrhagic transformation. Our aim is to assess the role of NLR as a predictor of functional outcome in patients with acute ischemic stroke after thrombolysis.

Methods:: A retrospective chart review of 98 patients who presented with acute ischemic stroke who received thrombolysis between 2015 and 2019 at a tertiary care setup in a developing country was done. A ratio between neutrophils and lymphocytes for all patients at admission and the mean values with standard deviation were calculated. Patients with an mRS of 0–2 were classified as a good functional outcome and with the mRS of 3–6 as a bad functional outcome. The mean NLC was compared using an independent student's t-test.

Results:: In our study most of our participants were male 60(61.2%) with mean age 58±6.4. At 3 months, a good functional outcome was seen in only 31 patients (31.6%). Of the patients with a good functional outcome, 19 (61.3%) were in group 1 and 12 (38.7%) were in group 2. Patients in Group 2 have a bad functional outcome (OR 2.7; 95% CI 1.11 to 6.39; p < 0.02).

Conclusions:: Our study revealed that patients who present with acute ischemic stroke who has a raised NLR at the time of administration of thrombolysis may have a poor functional outcome (mRS 3-6) at 3 months.
Background and Aims:: DAVF is an abnormal connection between arteries and veins, where blood is supplied to DAVFs mainly through branches arising from the external carotid artery. Common symptoms are headache, orbital bruit, pulsatile tinnitus, and ophthalmoplegia and acute intracranial hemorrhage. There are only a few reports of DAVFs presenting with dementia syndrome, and a decline in neurocognitive function.

Methods:: We present 2 patients presenting with history of multiple episodes of seizures and progressive behavioral and cognitive changes. The first patient presented with ptosis and ophthalmoplegia in the right eye, while the second patient presented with altered sensorium. Both had severe cognitive impairment, inattention and disorientation to time, place and person. In both, Digital subtraction angiography provided a definitive diagnosis of hypervascular Dural AV fistula at the right transverse sigmoid junction with arterial feeders from the right ECA and meningohypophyseal trunk of the ICA, with significant cortical venous hypertension noted.

Results:: Through a femoral access, both underwent transarterial embolization through the Middle Meningeal branch of the right External Carotid Artery using Onyx, resulting in complete occlusion of fistula and resolution of venous hypertension. Post embolisation, Cognitive function assessment revealed increased attention span and improved orientation with time, place and person.

Conclusions:: DAVF can be one of the rare but reversible causes of dementia. Early diagnosis and treatment may help to dramatically improve patients’ clinical condition and minimize long-term disability.
USEFULNESS OF MULTIMODAL CT PC-ASPECT CALCULATION IN INFRATENTORIAL STROKE

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\textsuperscript{1}University of Trieste, Clinical Unit Of Neurology, Department Of Medicine, Surgery And Health Sciences, University Hospital And Health Services Of Trieste – Asugi, University Of Trieste, Strada Di Fiume, 447, 34149 Trieste, Italy, Trieste, Italy, \textsuperscript{2}Cattinara University Hospital, ASUGI, University of Trieste, Trieste, Italy, Neurology Unit, Department Of Medical, Surgical And Health Sciences, Trieste, Italy, \textsuperscript{3}Radiology Unit, Radiology Unit, Department Of Medicine, Surgery And Health Sciences, University Hospital And Health Services Of Trieste – Asugi, University Of Trieste, Trieste, Italy

\textbf{Background and Aims::} Routine examinations for the diagnosis of posterior circulation stroke include clinical assessment using the National Institutes of Health Stroke Scale (NIHSS) and brain imaging, generally, non-contrast brain CT; both of them proved to be unreliable on detection of infratentorial strokes. We tested the validity and the prognostic value of posterior circulation Alberta Stroke Program Early CT Score (pc-ASPECTS) in patients with posterior circulation stroke calculated on noncontrat CT (NCCT), CT-angiography source images (CTA) and CT-perfusion (CTP) images.

\textbf{Methods::} Routine examinations for the diagnosis of posterior circulation stroke include clinical assessment using the National Institutes of Health Stroke Scale (NIHSS) and brain imaging, generally, non-contrast brain CT; both of them proved to be unreliable on detection of infratentorial strokes. We tested the validity and the prognostic value of posterior circulation Alberta Stroke Program Early CT Score (pc-ASPECTS) in patients with posterior circulation stroke calculated on noncontrast CT (NCCT), CT-angiography source images (CTA) and CT-perfusion (CTP) images.

\textbf{Results::} 50 patients with posterior cerebral stroke were enrolled. CTP showed abnormalities in 34 cases (68%), mainly involving cerebellum or occipital regions. The pc-ASPECT score calculated on NCCT, CTA and CTP had a sensibility of 72%. Pc-ASPECT calculated on MTT maps had the best correlation with NIHSS score at discharge, mRS at discharge and at 3 months ($p$=0.001, $p$=0.00, $p$=0.003).

\textbf{Conclusions::} we evaluated the usefulness of newly developed pc-ASPECTS on CTP in predicting functional outcome in acute posterior circulation ischemic stroke, and found that this appears be a powerful marker for predicting functional outcome.
Background and Aims:: Hyperglycemia is a known predictor of hemorrhagic transformation (HT) after ischemic stroke. However, it is unclear whether the association is due to diabetic hyperglycemia or stress hyperglycemia. We aimed to use the stress hyperglycemia ratio (SHR) to better determine the role of stress hyperglycemia in HT.

Methods:: Consecutive patients with ischemic stroke within 24 h of onset evaluated from January 2016 to September 2018 were included. SHR was calculated by admission random glucose divided by estimated average glucose derived from glycosylated hemoglobin. HT was rated on follow-up brain imaging and classified as hemorrhagic infarction (HI) and parenchymal hematoma (PH). Multivariable logistic regression was performed to evaluate the association between SHR and HT as well as its subtypes.

Results:: Among the 865 patients, 122 (14.1%) developed HT with 79 HI and 43 PH. Compared with the bottom tertile, patients in the top tertile of SHR were associated with an increased risk of HT after adjustment for confounders (OR 1.84, 95% CI 1.05–3.25, $P_{\text{trend}} = 0.036$). A multiple-adjusted spline regression model showed a dose-response relationship between SHR and HT. Subgroup analyses further confirmed the association. In multinomial regression analysis, SHR was significantly associated with PH rather than HI. The addition of SHR to conventional risk factors improved the prediction of HT (net reclassification improvement index = 22.48%, $P = 0.013$; integrated discrimination improvement = 0.61%, $P = 0.026$).

Conclusions:: Elevated SHR was related to HT after ischemic stroke. This may improve the stratification of HT risk in clinical practice or future trials targeting HT.
SHIFT FROM DRIP-AND-SHIP TOWARDS MOTHERSHIP MODEL FOR MECHANICAL THROMBECTOMY DURING COVID-19 PANDEMIC: A RETROSPECTIVE ANALYSIS OF A STROKE NETWORK PERFORMANCES.

Matteo Paolucci¹, Maria Ruggiero², Vanni Agnoletti³, Maurizio Menarini⁴, Raffaella Francesconi⁵, Tiziana Perin⁶, Andrea Fabbri⁷, Sara Biguzzi¹, Francesco Cordici⁸, Marco Longoni⁹
¹“M. Bufalini” hospital, Neurology, Cesena, Italy, ²“M. Bufalini” hospital, Neuroradiology, Cesena, Italy, ³“M. Bufalini” hospital, Intensive Care Unit, Cesena, Italy, ⁴AUSL Romagna, 118, Cesena, Italy, ⁵“M. Bufalini” hospital, Emergency Department, Cesena, Italy, ⁶“Infermi” Hospital, Emergency Department, Rimini, Italy, ⁷“Morgagni-Pierantoni” Hospital, Emergency Department, Forlì, Italy

Background and Aims:: The choice between transport of acute ischemic stroke patients to the nearest Primary Stroke Centers (drip-and-ship model) versus direct transport to the Comprehensive Stroke Center (mothership model) is still a matter of debate. We shifted from a drip-and-ship towards a mothership model during the first wave of COVID-19 pandemic in spring 2020. We retrospectively analyzed stroke network performances comparing the two models.

Methods:: All spoke-district patients treated with endovascular thrombectomy (EVT) between 15th March – 15th June 2019 (drip-and-ship) and 2020 (mothership) were included in the study. We compared call-to-door time (CDT), door-to-CT time (DCT), door-to-needle time (DNT), door-to-groin time (DGT), call-to-needle time (CNT) and call-to-groin time (CGT) between the two periods. We also compared functional independence (modified Rankin Scale, mRS) at 3 months.

Results:: 24 spoke-district patients in 2019 (drip-and-ship) and 26 in 2020 (mothership) underwent EVT. In 2020 a higher number of patients received IV thrombolysis in combination with EVT (p=.030). The groups did not differ for age, sex, risk factors, pre-stroke mRS 0-1, NIHSS and ASPECTS distribution. In 2020 we found longer CDT (+23 minutes, p<.005), but shorter DCT (-11.5 minutes, p=.017), DNT (-20.5 minutes, p=.001), and DGT (-78 minutes, p<.005). Overall, in 2020 we found a significant decrease in CGT time (-55.5 minutes, p<.005) without significant differences in CNT (p=.324). We found no effects of the stroke network model on the 3-month mRS (shift analysis, p=.241; mRS categories 0-1 vs 2-6, p=.706).

Conclusions:: The mothership model guaranteed quicker EVT without significantly delaying IVT.
IMPLANTABLE LOOP RECORDER TO DETECT ATRIAL FIBRILLATION IN CRYPTOGENIC STROKE: A REAL-WORLD EXPERIENCE

Arianna Manini, Giuseppe Scopelliti, Francesco Mele, Ilaria Cova, Pierluigi Bertora, Silvia Rosa, Marco Schiavone, Maurizio Viecca, Giovanni Forleo, Leonardo Pantoni

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Background and Aims: Paroxysmal atrial fibrillation (AF) represents one of the main mechanisms underlying cryptogenic stroke (CS). Trials have shown that prolonged cardiac monitoring through Implantable Loop Recorders (ILR) allows higher AF detection frequency after CS compared with routine follow-up and 24-hour Holter monitoring, reaching 30% rate at 3 years. We aimed at assessing whether these data are reproducible in clinical practice.

Methods: From July 03, 2018 to March 10, 2021, CS patients were implanted with ILR after that extensive testing (24-hour ECG monitoring, echocardiography, head and neck computed tomography angiography) had not revealed a definite stroke etiology. Exclusion criteria were anticoagulant therapy contraindication, scarce compliance, and short-term poor prognosis. ILR online transmissions were regularly checked by neurologists; arrhythmias alarms were reviewed by cardiologists.

Results: Out of 114 hospitalized CS patients, 86 (75.4%) (mean age 72.2 years, range 49–88) were subjected to ILR. Median follow-up time from implantation is currently 457 days (range 19–1000). AF was detected in 24/86 (27.9%) patients after a median time of 99.5 days (range 1–520). Three patients had ischemic stroke recurrence. In one case, AF was not detected; one had ischemic stroke recurrence caused by internal carotid artery plaque after five months from AF diagnosis and anticoagulation start; the third was waiting for anticoagulants starting after AF diagnosis.

Conclusions: ILR is feasible and effective to detect occult AF after CS in clinical practice, with higher sensitivity compared to short-term monitoring. Our results suggest that up to 30% of CS patients may have AF as underlying stroke etiology.
MULTIPLE VASCULAR EVENTS REVEALING VARICELLA-ZOSTER VIRUS VASCULOPATHY, THE IMPORTANCE OF THE MEDICAL HISTORY: CASE REPORT

Roukya Benkhadra, Biljana Djurisic, Kosta Vassilev, Sophie Dupont
Pitié Salpêtrière Hospital, Neurological Rehabilitation, PARIS, France

Background and Aims:: Varicella-zoster virus (VZV) usually causes localized zoster in adults. However, in immunocompromised patients, it can cause systemic manifestations. Early diagnosis and therapy are crucial for the prognosis of the patients. To raise awareness of the diagnosis of VZV vasculopathy and the importance of looking for signs of previous infection up to 12 months.

Methods:: We report the case of an 85 year old lady, with a history of ophthalmic zoster who presented numerous vascular events with a progressive neurological worsening.

Results:: An 85 year old women presented in December 2018, an ischemic stroke of the right middle cerebral artery which was thrombolysed. An intracranial stent was also placed with a favorable evolution. An atheromatous cause was retained. Additionally, a pulmonary and mediastinal tuberculosis was diagnosed. Her neurologic condition was continuously worsening with cognitive impairment. In April 2019, she presented a right post traumatic subdural hematoma. But the evolution was marked by the occurrence of a contralateral subdural hematoma. Three days later she developed an ischemia of the right lower limb and died shortly. Looking back to her medical history we found a right ophthalmic Herpes Zoster in May 2018. The keypoint of this case is that this immunocompromised patient had ipsilateral ophthalmic herpes zoster 6 months before the stroke, a progressive neurological worsening despite all the treatment. The most likely hypothesis is a VZV vasculopathy, after the exclusion of any other etiology.

Conclusions:: Systemic VZV vasculopathy, can cause serious complications, with diverse clinical manifestations. Early detection and proper treatment is crucial.
RECURRENT SUBCORTICAL INFARCTS, INTRACRANIAL HYPERTENSION AND ASEPTIC MENINGITIS: POSSIBLE NEUROSARCOIDOSIS? A CASE REPORT

Pietro Anceschi, Alessia Fiore, Stefania Lazzari, Elisabetta Chierici, Lucia Zinno, Irene Florindo
Neurosciences Unit, Department Of Medicine And Surgery, University Of Parma, Parma, Italy

Background and Aims:: Neurosarcoidosis (NS) is a rare etiology of small-vessel-vasculitis of CNS. Even if the majority of cases shows systemic extraneural inflammation, a small percentage of patients (10-19%) manifests a disease isolated to CNS, making histological confirmation difficult to obtain. Various disease presentation and lack of relevant diagnostic tests contribute to diagnostic challenge.

Methods:: We describe the case of a 47-years-old African man with subacute onset of headache, fatigue, serotine low-grade fever, asymmetric spastic paraparesis and intention tremor.

Results:: Inflammation rates (ESR, C-reactive protein) were increased. Subsequent brain MRI showed recurrent subcortical infarcts suggesting a small-vessel-vasculitis. Angio-MRI didn’t reveal any vascular pathology. CSF opening pressure was elevated with mononuclear pleocytosis, hyperproteinorrachia, hypoglycorrhachia and oligoclonal bands (mirror pattern) on chemical examination. CSF cytological and microbiological analysis including PCR-based assay for Mycobacterium were negative. Chest HRCT and total-body FDG-PET didn’t find any signs of extra-CNS involvement apart from diffuse mild lymphadenopathy, not typical for lymphoma and too small for biopsy. Ocular evaluation was normal. TE Echocardiography revealed a hypertrophic cardiomyopathy. Enzymatic assay for Fabry disease is ongoing. Assuming NS as a probable cause, the patient underwent a high dose steroid treatment with immediate disappearance of headache and fatigue. Clinical and radiological follow-up are in progress.
Conclusions: The case highlights sarcoidosis as a possible etiology of isolated small-vessel-vasculitis of CNS, given the absence of clear-cut extraneural involvement. If contraindications are excluded, therapeutical attempt can be considered even when a validation biopsy is unfeasible.
POSTSTROKE DEPRESSION INCIDENCE AND CORRELATED FACTORS IN A DEVELOPING COUNTRY POPULATION: A PROSPECTIVE STUDY

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¹Jordan University of Science and Technology, Department Of Neurology/faculty Of Medicine, Ar Ramtha, Jordan, ²University of Oxford, Department For Continuing Education, Oxford, United Kingdom, ³Jordan University of Science and Technology, Clinical Pharmacy, Irbid, Jordan

Background and Aims:: Poststroke Depression (PSD) is a well-recognized psychological disorder affecting patients after suffering from either a hemorrhagic or ischemic stroke. PSD have serious repercussions on stroke survivors rehabilitation and recovery process. This study objective is to assess the incidence rate and the factors associated with developing PSD among Jordanian stroke patients.

Methods:: A 151 acute stroke patients were recruited for follow-up after their admission to the neurology ward at a tertiary teaching hospital. The sociodemographic characteristics, clinical features and other related variables were collected upon admission. Stroke outcome was identified by one-month modified Rankin score (mRS) and Barthel Index (BI) scores. PHQ-9 Scale was used to establish the diagnosis of PSD for those scoring five or more. Furthermore, a logistic regression analysis was conducted to assess for significant predictors.

Results:: The incidence rate of PSD was found to be 15% (on admission), 24.83% (on one month), and 17.39% (on 3 months). Severity was noted to correlate increasingly with time, as the incidence of severe PSD was 1% (on admission), 2.13% (on one month), and 6.52% (on 3 months). PSD was correlated significantly with coexisting chronic kidney disease (P= 0.007), current smoking status (P=0.002), moderate or severe disability (mRS score) at stroke onset (P=0.014), and severe dependency (BI) after one month (P= 0.031).

Conclusions:: In Jordanian stroke survivors the highest incidence of PSD (24.8%) was noted after one month, while sever PSD was highest after three months.
COGNITIVE IMPAIRMENT AT 30 DAYS IN FIRST-EVER STROKE SURVIVORS

Khadija Sonda Moalla¹, Mariem Damak¹, Olfa Chakroun², Olfa Hdiji¹, Salma Sakka¹, Sawsan Daoud¹, Nadia Bouattour¹, Nouha Farhat¹, Noureddine Rekik², Chokri Mhiri¹
¹Universal Hospital Habib Bourguiba, Neurology, SFAX, Tunisia, ²Universal Hospital Habib Bourguiba, Emergency, SFAX, Tunisia

Background and Aims:: Functional assessment in stroke survivors is mostly limited to motor abilities, with cognitive assessment largely omitted. We sought to analyze the frequency of cognitive impairment (CI) in stroke survivors and its prognostic relationship at 1 month after the initial event.

Methods:: We assessed first-ever stroke survivors 30 days after the event by the mini-mental state examination (MMSE). Patients with a stroke recurrence during the follow-up were not included. The distribution of MMSE scoring was analyzed according to functional categories as determined by the Modified Rankin Scale (mRS).

Results:: A total of 161 stroke survivors (57.8% men, median age 67.7 years, interquartile range: 24–96 years) received cognitive assessment by MMSE [mean: 20.65 points, standard deviation (SD): 7.3 points]. The mean MMSE score was progressively lower in patients with mRS 0–1 (23.4, SD: 6.9 points), mRS 2–3 (19.7, SD: 6.6 points) and mRS 4–5 (15.45, SD: 6.3 points) (p < 0.001). Moreover, the frequency of cases with MMSE <22 was significantly higher as motor disability increased, but remarkably, patients with a very good functional status (mRS 0–1) also had a high frequency of suboptimal performance (<22 points) on the MMSE (mRS 0–1: 32.4%, mRS 2–3: 38.2%, mRS 4–5: 29.4%, p < 0.001). A similar situation was observed with MMSE <16 points (mRS 0–1: 30%, mRS 2–3: 30%, mRS 4–5: 40%, p=0.004).

Conclusions:: Despite the limitations of MMSE as screening tool of the mental function in patients with cerebrovascular injury, it is clear that CI occurs after a first-ever stroke, even in subjects without significant motor disability.
DETECTION OF CEREBRAL MICROEMBOLISM BY A MODERN TECHNIQUE OF ACUTE ISCHEMIC STROKE WITH CONFIRMED CORONAVIRUS DISEASE (COVID-19)

Aziz Umirov
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Background and Aims:: The aim of this study was to examine the detection of cerebral microembolism by a modern technique of acute ischemic stroke with confirmed coronavirus disease (COVID-19).

Methods:: We studied 10 people who had an acute ischemic stroke in the Department of Neurology at the TMA. All patients with confirmed COVID-19 who underwent clinical TCD ultrasound to detect microembolism were included.

Results:: A total of ten TCD studies were conducted in eight COVID-19 patients (5 men and 3 women, mean age 65 ± 5 years), five with confirmed ischemic stroke and three with refractory encephalopathy. Microembolism were found in four male patients, three patients had a confirmed ischemic stroke, and two developed long-term encephalopathy. Microemboli of varying severity were detected in multiple vascular areas in four patients, and in the second patient, microemboli persisted despite therapeutic anticoagulation. Of five patients without signs of microembolism on ultrasound of TSD, two patients had a confirmed ischemic stroke, and three remained refractory encephalopathy.

Conclusions:: Ultrasonography (TCD) to detect microemboli identified five confirmed COVID-19 patients with signs of cerebral arterial microembolism, including two who received therapeutic anticoagulants. TCD ultrasonography is a non-invasive method for assessing cerebral microembolism in patients with COVID-19 and may be useful to assess the response to treatment in cases of suspected and impaired hypercoagulability. Further studies investigating the prevalence of cerebral microembolism and associated risk factors to characterize their pathogenetic mechanism and guide therapeutic interventions in hospitalized COVID-19 patients.
MULTIPLE EMBOLIC INFARCTIONS IN A CASE OF A PARANEOPlastic SYNDROME CAUSED BY HEPATOCELLULAR CARCINOMA

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Background and Aims:: Patients with polycythemia are at high risk for ischemic events including ischemic stroke. Secondary polycythemia is one of the manifestations of paraneoplastic syndrome of hepatocellular carcinoma. Increased red blood cells can elevate blood viscosity causing individuals susceptible to ischemic events.

Methods:: We present a case of a patient who visited the Emergency Department with right leg weakness suggestive of the left anterior cerebral artery infarction.

Results:: MRI showed multiple small nodular and fragmented acute embolic infarctions at the both internal border zone and corpus callosum. On admission, he was found to have elevated hemoglobin, hematocrit, and total cholesterol. Serum erythropoietin was also elevated. An abdominal CT scan revealed heterogeneous enhanced 2 masses in the right liver, compressing the main portal vein, about 12cm, and 1.5cm respectively with several prominent lymph nodes in the gastrohepatic ligament, suggestive of malignant masses. There was a marked elevation of tumor markers for hepatocellular carcinoma such as α-fetoprotein (AFP) and protein induced by vitamin K absence II (PIVKA-II). Needle biopsy of the hepatic lesion showed moderately differentiated hepatocellular carcinoma with a trabecular pattern. The patient was treated with antiplatelet agents during the acute stage and regained right leg motor function only with right foot drop.

Conclusions:: Elevated blood viscosity is associated with vaso-occlusive events including ischemic stroke. This case suggests that acute ischemic stroke could be an initial symptom of a paraneoplastic syndrome caused by hepatocellular carcinoma. It is needed to check erythropoietin level for the evaluation of ischemic stroke patients with polycythemia for detecting underlying cause.
THYROID DYSFUNCTION – AN INDEPENDENT RISK FACTOR FOR ISCHEMIC STROKE IN YOUNG ADULTS?

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Background and Aims:: Various studies plead for the association between thyroid dysfunction and cerebrovascular disease, not only as a result of subsequent atrial fibrillation and cardioembolic stroke. Among the mechanisms incriminated are the increased adrenergic activity, the elevated levels of reactive oxygen species, the hemodynamic changes, and the coagulopathies found in hyperthyroidism whereas, in hypothyroidism alterations in lipids metabolism, in the arterial muscle structure, and a greater risk for atherosclerosis are described. The question is if thyroid dysfunction increases the risk of acute ischemic stroke.

Methods:: We analyzed the cases of two patients admitted for acute ischemic stroke, one presenting subclinical hypothyroidism due to autoimmune causes and one overt hyperthyroidism. They were both females, under 55 years old, previously undiagnosed, and untreated for thyroid dysfunction. Clinical, biological, and imaging investigations were made to establish the cause of the stroke, no apparent explanation being found.

Results:: The MRI imaging revealed that the patient with hyperthyroidism presented a left frontotemporal ischemic stroke, while the one with hypothyroidism had a small, left, pontine ischemic lesion. After extensive investigations, finding no causative factor for the onset of the strokes raised the possibility of an association between the underlying thyroid disease and the cerebral infarction.

Conclusions:: Although not many existing studies find the relationship between the dysfunction of the thyroid and the ischemic stroke significant, the clinical findings from our cases lead to the plausibility of this association.
INTRACEREBRAL HAEMORRHAGE (ICH) EVACUATION BY MINIMALLY INVASIVE NEUROSURGERY (MIN) TECHNIQUES

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Background and Aims:: Evaluation of a minimally invasive ICH-evacuation series. Describing a cheap and fast method, that can be learned everywhere.

Methods:: More than 260 patients underwent this application by the presenting author. A series of the 56 recent cases, 26 female and 29 male, 69.1 y (40 - 83) (1 child excl.), was analyzed This MIN concept combined several key-techniques to assist microsurgery: mouth-tracked high-zoomed Microscope, Neuro-Endoscopy, Neuro-Ultrasound, LASER and Sealing.

Results:: Compared with STICH I, the favorable outcome was pushed from 26.1% to 86.0%. In nearly all cases it was possible to evacuate the complete hematoma within 1 hour, and the hematoma evacuation decreased the ICP always fast to normal levels. Clinical results were excellent in lobar bleedings with isochoric before surgery. Large and deep-seated hemorrhages needed longer recovery time, but in all cases postop CT showed fast reduction of perifocal edema and ICP -levels.

Conclusions:: Combination of ultrasound, mouth tracking, endoscopy, LASER and sealing technique enabled evacuation of all type of hematoma minimal invasively and very effectively within one hour. Ultrasound real-time control detected all types and locations of bleeding causes (aneurysms, angiomas, cavernomas, tumors and origin of bleeding). The evacuation amount and the reaction of the brain were under visual real-time control. Mouth tracking enables maximal-zoomed, and free hands fast acting for safe operative control. The method is cheap, fast, and can be learned during regular training. Ref.: KDM Resch, Key Concepts in MIN Vol. 1, 2020; Vol. 2, 2021 (in press)/ Springer, Heidelberg
MECHANICAL THROMBECTOMY IN STROKE AND THE AVAILABILITY OF THE ENDOVASCULAR TEAM DURING INSTITUTIONAL EMERGENCY SERVICE - THEORY VERSUS REALITY

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Background and Aims:: Mechanical thrombectomy (MT) is the standard treatment for stroke in occlusion of a large endovascularly accessible artery. The topic discussed is the permanent presence of the endovascular team in the center 24/7 to reduce delays until the beginning of MT.

Methods:: 355 patients who underwent MT for large artery occlusion in 2018-2019 from Comprehensive stroke center (CSC) were analyzed retrospectively. The data were confronted with theoretical assumptions according to the calendar share of working hours and the total annual time fund.

Results:: The period of institutional emergency service according to calendar data in the Czech Republic is approximately 76% of the time of the year. This value was chosen as the most pessimistic value of the number of patients potentially admitted in the absence of the endovascular team (with a concomitant 100% admission of patients by primary transport to the CSC). 355 patients treated with MT in CSC (171 in 2018 and 184 in 2019) were analyzed. At the time of institutional emergency service, 227 patients (63.9 %) were admitted. However, in the absence of the endovascular team at the time of institutional emergency service, there were only 58 patients (16.3 %). In the next steps, this number could be reduced below 5%.

Conclusions:: Even with the impossibility of establishing the presence of an endovascular team in the center in the 24/7 mode, it is possible to reduce the number of patients admitted during the absence of the team below 5%.
Background and Aims:: We present a case of acute ischemic stroke (AIS) in a pregnant woman treated with recombinant tissue plasminogen activator (rt-PA) and mechanical thrombectomy (MT).

Methods:: A 33-years-old woman at 5 weeks gestation referred to emergency room 1 hour after developing dysarthria, left hemiplegia and anesthesia of the left limbs (NIHSS=14).

Results:: CT angiography revealed a right M1 segment occlusion. The patient underwent IV rTPA and then was subjected to MT with good reperfusion of cerebral blood flow. Extensive diagnostic workup was unremarkable except for evidence of patent foramen ovale. A medical physics evaluation showed an estimated total dose of radiations acquired of 1,26 mGy. Neurological condition improved with residual mild paresis and hypoesthesia of the left arm at dismissal (NIHSS=3). The pregnancy is ongoing, but an extensive gynecologic exam ruled out intrauterine or foetal complications. The effectiveness and safety profile of thrombolytic agents and MT in pregnant women is not known as these patients have been excluded from reperfusion trials. Rt-PA does not cross the placenta, but maternal hemorrhagic complications and abortion have been reported. MT raises concerns regarding radiation exposure and the use of iodinated contrast agents during the procedure. Few cases of pregnant women treated with MT ± IV rt-PA have been reported with positive outcomes for both mother and fetus.

Conclusions:: IV rt-PA and MT may be effective and safe treatments for pregnant patients. Precautions need to be taken to reduce the foetal radiation exposure and the dose of iodinated contrast agents.
Liver fibrosis indices associated with hematoma expansion in patients with intracranial hemorrhage

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Background and Aims:: Liver fibrosis may cause subclinical coagulopathy and endothelial dysfunction, which link to hematoma expansion (HE) after intracerebral hemorrhage (ICH). We evaluated the association between liver fibrosis indices and HE in a Chinese population with primary ICH.

Methods:: We performed a retrospective review of data from 438 consecutive patients with primary ICH who had admission laboratory data and neuroimaging data to calculate HE (>33% or >6 mL). Selected liver fibrosis indices include aspartate aminotransferase (AST)-platelet ratio index (APRI), (AST/alanine aminotransferase ratio [ALT])/platelet ratio index (AARPRI), Fibrosis-4 (FIB 4), modified Fibrosis-4 (mFIB 4), fibrosis quotient (FibroQ) and Forns Index. The association of fibrosis indices with HE was assessed using multivariable logistic regression analyses. The patients with HBV infection were performed in a sensitivity analysis.

Results:: Of 438 patients with primary ICH, 117 (26%) had HE. After adjusting baseline hematoma volume, APRI (odds ratio [OR], 1.62 [95% CI, 1.01-2.59]), AARPRI (OR, 1.26 [95% CI, 1.00-1.57]) and FIB 4 (OR, 1.15 [95% CI, 1.02-1.30]) were independently associated with HE after ICH. Also, in patients with ICH complicated with HBV infection, AARPRI (OR, 1.39 [95% CI, 1.06-1.81]), FIB 4 (OR, 1.19 [95% CI, 1.03-1.39]), mFIB 4 (OR, 1.07 [95% CI, 1.00-1.13]) and FibroQ (OR, 1.06 [95% CI, 1.00-1.11]) were associated with HE.

Conclusions:: Therefore, two liver fibrosis indices (AARPRI and FIB 4) were independently related to HE after ICH, regardless of whether HBV infection is present. This finding may represent a potential therapeutic target. Future prospective larger studies are needed to confirm our findings.
CT PERFUSION ASPECTS PREDICTS FINAL ISCHEMIA EXTENT IN PATIENTS WITH STROKE BEYOND 6 HOURS AFTER SYMPTOMS ONSET.

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Background and Aims:: The Alberta Stroke Program Early Computed Tomography Score (ASPECTS) has been previously applied to perfusion CT (CTP). We investigated the capability of CTP-ASPECTS to predict final ischemia extent in patients with stroke beyond 6 hours after symptoms onset.

Methods:: We reviewed prospectively collected data from stroke patients with internal carotid artery and/or M1-segment middle cerebral artery occlusion who performed CTP between 6 to 12 hours after symptoms onset. We identified patients with complete recanalization after thrombectomy and patients who have not received revascularization treatment. Using ordinal regression, we estimated the predictive effect of cerebral blood volume (CBV)-ASPECT and mean transit time (MTT)-ASPECTS on 24-hour ASPECTS (0 to 10) by calculating the odds ratios (ORs) with two-sided 95% confidence intervals (CI) after adjustment for baseline ASPECTS and onset-to-imaging time.

Results:: Of the 12 patients with complete recanalization after thrombectomy, median value was 9 (IQR 9-10) for baseline ASPECTS, 10 (IQR 9-10) for CBV-ASPECTS, 8 (IQR 5-9) for MTT-ASPECTS, and 8 (IQR 5-10) for 24-hour ASPECTS. Of the 18 patients who have not received revascularization treatment, median value was 9 (IQR 8-10) for baseline ASPECTS, 10 (IQR 9-10) for CBV-ASPECTS, 8 (IQR 5-9) for MTT-ASPECTS, and 8 (IQR 7-9) for 24-hour ASPECTS. CBV-ASPECTS predicted 24-hour ASPECTS in patients with complete recanalization (OR 4.590, 95% CI 1.038-20.292), while MTT-ASPECTS predicted 24-hour ASPECTS in patients who have not received revascularization treatment (OR 1.799, 95% CI 1.042-3.106).

Conclusions:: CTP-ASPECTS predicts final ischemia extent in patients with stroke beyond 6 hours after symptoms onset.
A NOVEL HOME PATIENT TELEMONITORING SYSTEM FOR POST-ACUTE TIA/MINOR STROKE: AN EXPERIENCE DURING COVID-19 PANDEMIC

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**Background and Aims:** Telemonitoring solutions may assure patients' safety in the TIA/stroke post-acute phase outside the hospital. Currently there is a lack of a multi-parametric telemonitoring system for early post-acute TIA/stroke patients, in particular potentially useful in COVID-19 emergency period. We aimed to design and test a comprehensive e-Health system based on a multiparametric telemonitoring solution in this fragile group.

**Methods:** We proposed a novel e-Health system and performed a preliminary evaluation of a 14-day telemonitoring protocol for TIA/minor stroke during COVID-19 emergency. The proposed system involves the use of portable devices for BP/HR/SpO2/temperature sensing, panic-button and a dedicated informatic platform.

**Results:** Eight consecutive TIA/minor stroke patients were included in the proof-of-concept validation test. A mean of 32 exceeding threshold events for each patient was observed. 52% of alarms were related to BP, 34% to HR, 9% to lower SpO2 and 5% to higher body-temperature. In 7 out of 8 patients the clinician changed the prescribed therapy, in particular the neurologist modulated the antihypertensive therapy. 6 out of 8 patients had a normalization of all parameters in the last two days of study period. We observed a significant improvement of quality of life, as well as a significant reduction of anxiety and depression status. The 3-month follow-up showed total adherence of prescribed therapy and no stroke/TIA recurrence or other emergency department admissions.

**Conclusions:** The proposed telemonitoring solution allowed to promptly and remotely identify vital sign alterations at home during the early post-acute phase, allowing therapy and behavioral intervention adjustments.
EEG SPECTRAL PARAMETERS CORRELATE WITH THE EXTENT OF BRAIN ISCHEMIA IN HYPER-ACUTE ISCHEMIC STROKE

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Background and Aims:: Brain electrical activity alterations in acute ischemic stroke are related to neurophysiological changes during hypoperfusion as manifestation of neurovascular coupling. EEG could be applicable for bedside functional monitoring in the hyper-acute phase of ischemic stroke. This study aimed to investigate the relation between EEG changes and ischemic core-penumbra CT Perfusion (CTP) volumes, and their association with neurological deficit in the hyper-acute phase of ischemic stroke.

Methods:: CT Perfusion imaging and EEG recordings, measured with bedside wireless-EEG, were performed at admission in thirty-one ischemic stroke patients within 4.5 h from symptom onset. Ischemic core and total hypoperfused volumes were estimated from calculated CTP maps. Spectral parameters were extracted from EEG recordings. Correlation between ischemic volumes and EEG spectral parameters were investigated. In addition, we investigated the association of EEG and CTP parameters with neurological deficit measured by NIHSS.

Results:: The significant positive correlations were observed between ischemic volumes (core volume and total ischemic volume) and EEG spectral parameters: delta/alpha ratio (DAR), (delta + theta)/(alpha + beta) ratio (DTABR) and relative delta power, while the relative alpha power correlated inversely both with core volume and total ischemic volume. The identified EEG parameters, as well as CTP volumes, showed significant relation with NIHSS.

Conclusions:: The results showed that quantitative EEG can be a possible complementary tool in the evaluation of stroke severity and monitoring of the brain ischemia evolution in hyper-acute phase.
LIVER FIBROSIS-4 SCORE PREDICTS HAEMORRHAGIC TRANSFORMATION IN ISCHEMIC STROKE UNDERGOING MECHANICAL THROMBECTOMY.

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Background and Aims:: Haemorrhagic transformation (HT) of brain infarct is a complication of acute ischemic stroke, and may be induced or favoured by reperfusion therapy. The Fibrosis-4 (FIB-4) score is one validated index to assess the extent of liver fibrosis. The aim of this study was to assess the validity and accuracy of the FIB-4 score as a predictor of HT in patients with ischemic stroke treated with mechanical thrombectomy.

Methods:: We retrospectively identified consecutive acute ischemic stroke patients hospitalized at the Stroke Unit of the Marche Polytechnic University, Ancona, Italy, who underwent mechanical thrombectomy, with or without intravenous thrombolysis. The FIB-4 score was computed for every patient, as follows: FIB-4 = (Age × AST) / (PLT × \sqrt{ALT}) The study endpoint was the occurrence of HT as detected by routine brain CT or MRI performed within 72 hours. Predictive performance of the FIB-4 index was investigated through logistic regression and discrimination test.

Results:: Out of the 162 included patients, HT occurred in 72 (43.64%) patients. The median FIB-4 score was significantly higher among patients who developed HT than those without HT. The FIB-4 score was an independent predictor of HT [adjustedOR = 2.877, 95% confidence interval 1.006-8.224, P = 0.049] after the adjustment for potential confounders. It showed good discriminatory power with an area under the ROC curve of 0.910 and yielded a sensitivity of 73.3% and a specificity of 91.2%).

Conclusions:: The FIB-4 score was a significant predictor of HT and showed high predictive accuracy in patients with acute ischemic stroke undergoing mechanical thrombectomy.
ASSESSMENT OF CEREBRAL VASOMOTOR REACTIVITY IN PATIENTS WITH ACUTE STROKE AND TRANSIENT ISCHEMIC ATTACK (TIA) WITH DIFFERENT ETIOPATHOGENESIS: PRELIMINARY RESULTS

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**Background and Aims:** An impaired vasomotor reactivity (VMR) represents a negative prognostic factor for vascular and degenerative cognitive deterioration. Only few studies have addressed VMR in acute phase of stroke. We aim to investigate if VMR, calculated through the breath holding index (BHI), is a prognostic marker of clinical outcome in stroke/TIA patients.

**Methods:** In this longitudinal observational study (January 2020-2023) we enroll patients with acute mild stroke or TIA of anterior circulation with NIHSS < 8. The study observation period of 12 months includes 4 assessments: T1 (48-72h from stroke onset), T2 (1 month follow up (FU)), T3 (6 months FU) and T4 (12 months FU). Clinical scales and cognitive tests are performed every time. VMR is evaluated at T1 and T3.

**Results:** From January 2020 to March 2021, 48 patients (63% men) with a median age of 69 (53.8-73.3) years were enrolled. 75% had a stroke. The median NIHSS was 2 (1-4) at onset. The median pre-mRS was 0 (0) while the median mRS was 1 (0-1) at baseline. We found an inverse correlation between the adjusted mean MMSE and Pulsatility Index (PI) of Middle Cerebral Artery (MCA) (p=0.039) and PI of Posterior Cerebral Artery (PCA) (0.037) and between the mean MOCA and PI of MCA (p=0.020) and PI of PCA (p=0.004) at baseline. 39 patients performed T2 evaluation, 25 T3 evaluation and 6 of them were evaluated at T4.

**Conclusions:** These are the preliminary results of our ongoing 3-year clinical observation and VMR evaluation of stroke/TIA patients admitted at our Neurology Unit.
INCIDENCE AND MORTALITY OF STROKE IN ULAANBAATAR, MONGOLIA: EARLY RESULTS OF A POPULATION-BASED STROKE REGISTRY

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Background and Aims:: Mongolia has one of the highest stroke rates in the world but there have not been any population-based registry data since 1999. We aimed to provide current stroke epidemiological data from a prospective registry among adult residents of the capital Ulaanbaatar (UB), Mongolia.

Methods:: All first-ever strokes in adults (≥18 years) from 3 suburbs of UB from 1 January 2019 to 31 December 2019 were registered. Surveillance according to WHO STEP methods to include all hospitals including state, district, private and family, forensic medicine center, general authority for state registration, and emergency medical services. According to CT/MRI/autopsy findings, strokes were categorized as ischemic stroke (AIS), intracerebral hemorrhage (ICH), subarachnoid hemorrhage (SAH), and stroke of undetermined type (UND).

Results:: A total of 878 first-ever stroke cases have been documented. After excluding duplicate cases and patients, 764 cases were included. Crude incidence and mortality rates are 132 and 65 per 100 000 person-years, respectively. Among all cases, AIS constituted 45.3%, ICH 42.5%, SAH 8.5%, and UND 3.7%, respectively. AIS:ICH ratio was 1.06. Age-specific rates in men (129/100000) aged ≥40 years was significantly greater than in women (81/100000) (P<0.001).

Conclusions:: Our study has established a comprehensive stroke surveillance system, which will expand to all of UB and include 12-months follow-up of a broad range of health outcomes to provide a contemporaneous assessment of stroke burden in Mongolia.
NEUROPROTECTIVE POTENTIAL OF HESPERETIN PHARMACOLOGICAL POSTCONDITIONING AGAINST CEREBRAL ISCHEMIC REPERFUSION INJURY IN MICE

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Background and Aims: Cerebral ischemic reperfusion injury results in neuronal destruction during the period of ischemia due to the deprivation of oxygen and energy. Pharmacological post conditioning is playing road map for neuroprotection. The present study has been designed to investigate the neuroprotective potential of Hesperetin-pharmacological post-conditioning against cerebral ischemic reperfusion injury in mice.

Methods: There was five group in the present study and each group having seven mice. The protocol no. is USPS/IAEC/CPCSEA/2020/Protocol No. 45. Bilateral carotid artery occlusion (BCAO) for 12 min followed by reperfusion for 24 hours was given to induced cerebral injury in Lacca mice. Hesperetin (50mg/kg and 100mg/kg i.p) was administered 30 min prior to global cerebral ischemia and ischemic post-conditioning (IPost). Memory were assessed using morris water maze test, degree of motor incoordination was evaluated using rota-rod and actophotometer employed to evaluate the locomotor activity of experimental animals. In addition, oxidative parameters were also estimated.

Results: BCAO followed by 24 hours’ reperfusion produced a significant loss of memory, motor dysfunction along with impairment of locomotor activity. I/R injury significantly increased thiobarbituric acid reactive substances level and decreased the glutathione level as well superoxide dismutase level. Ischemic & Pharmacological post-conditioning with Hesperetin significantly restored the memory impairment, motor dysfunction, locomotor activity and altered biochemical levels which were assessed by behavior, oxidative stress parameters (TBARS, SOD & reduced form of Glutathione) and histopathological examinations.

Conclusions: The neuroprotective effect of pharmacological post-conditioning in the current study may be via activation of eNOS followed by activation of cGMP and down regulation of MPTP.
EXPRESSIVE APHASIA AND HORIZONTAL GAZE Palsy FOLLOWING A RIGHT INTERNAL CAPSULAR AND GLOBUS PALLIDAL ISCHAEMIC STROKE: A CASE REPORT

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Background and Aims: Expressive (non-fluent) aphasia is commonly attributed lesions involving the dominant posterior inferior frontal cortex which includes the Broca’s area. Horizontal gaze palsies are mainly due to lesions either in the contralateral frontal cortex or the ipsilateral pons. A gaze palsy with ipsilateral paraparesis is usually due to a lesion in the frontal eye field. Gaze palsies are not described in subcortical infarcts whereas subcortical aphasia is a field under evaluation. We describe a case of acute ischaemic stroke involving the right internal capsule and the globus pallidum which resulted in left hemiparesis, left gaze palsy and expressive aphasia.

Methods: A 65-year-old left-handed male presented with acute onset left sided face, arm, leg weakness, left sided gaze palsy (involving saccadic movement) and expressive aphasia for 1 hour duration. After excluding an intra-cerebral haemorrhage, he was medically thrombolysed with poor clinical resolution.

Results: The diffusion weighted MRI brain done within 24 hours of stroke onset revealed an acute infarction with diffusion restriction in the right internal capsule and the globus pallidus region. There was no evidence of cerebral oedema or haemorrhagic transformation. The clinical deficits were the same by the end of one week.
Conclusions: Gaze palsies and aphasias can be seen in internal capsular infarcts in some patients. Gaze palsy could be due to the involvement of fronto-mesencephalic fibres traversing through the genu and the posterior limb of the internal capsule. Speech is a complex neurological process involving many cortical and subcortical structures. Subcortical strokes can lead to expressive aphasias as seen in this patient.
FASTING AND NON-FASTING TRIGLYCERIDES PROFILES IN ACUTE ISCHEMIC STROKE PATIENTS

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Background and Aims:: The prevalence and clinical implications of elevated fasting triglycerides (FTG) and non-fasting triglycerides (NFTG) in acute ischemic stroke (AIS) patients remain unknown. We aimed to elucidate the correlation of FTG and NFTG levels in AIS patients, and the clinical significance of elevated FTG and NFTG.

Methods:: Based on a multicenter prospective stroke registry, we identified AIS patients hospitalized within 24 h of onset with available NFTG results. The primary outcome measure was a composite of stroke recurrence, myocardial infarction, and all-cause mortality up to one year after stroke onset.

Results:: This study analyzed 2,176 patients. The differences between non-fasting and fasting lipid profiles according to intervals between the last mealtime and sampling time were significant only for TG. The prevalence of fasting and non-fasting hypertriglyceridemia was 11.5% and 24.6%, respectively. Multivariate analysis revealed that younger age, diabetes, and higher body mass index and initial systolic blood pressure were independently associated with both fasting and non-fasting hypertriglyceridemia (all p<0.05). Patients with higher quartiles of NFTG were more likely to be male, younger, ever-smokers, and diabetic, and have a family history of premature coronary heart disease and stroke (all p<0.05). Similar tendencies were observed for FTG. The composite outcome was not associated with FTG or NFTG quartiles.

Conclusions:: Our study showed that fasting and non-fasting hypertriglyceridemia are prevalent in AIS patients and show similar clinical characteristics and outcomes. High FTG and NFTG levels were not associated with occurrence of subsequent clinical events up to one year.
FIBRINOGEN DEPLETION AND INTRACEREBRAL HEMORRHAGE AFTER THROMBOLYSIS FOR ISCHEMIC STROKE: A META-ANALYSIS

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Background and Aims:: Intracerebral hemorrhage (ICH) can be a fatal complication of intravenous thrombolysis (IVT) for acute ischemic stroke. An early coagulopathy can develop after IVT, in relation to a significant fibrinogen depletion, increasing the risk of ICH. This systematic review and meta-analysis aimed at defining the role of fibrinogen depletion after IVT on the risk of ICH after IVT.

Methods:: Protocol was registered with PROSPERO (CRD42020124241) and followed PRISMA and MOOSE guidelines. We systematically searched English studies reporting rates of post-IVT ICH depending on fibrinogen depletion until 7/1/2021. Primary outcome was symptomatic ICH (sICH). Meta-analysis followed random-effect model to account for heterogeneity in design and timing of ascertainment. Bias were assessed via Newcastle-Ottawa Scale.

Results:: Overall, among 352 records identified, 5 observational studies were eligible for quantitative synthesis (n=2142), all of fair quality. Considering sICH within 24-36 h post-IVT, pooling data from 4 studies (n=1753) fibrinogen depletion consistently increased the risk of sICH (OR 3.67, 95%CI 2.28-5.90, p heterogeneity=0.55). Pooling adjusted estimates for age, gender and NIHSS from 3 studies (n=723), fibrinogen depletion was confirmed to significantly increase the risk of ICH after IVT (OR 5.41, 95%CI 2.96-9.89).

Conclusions:: Fibrinogen depletion significantly increases the risk of ICH after IVT for acute ischemic stroke. Routine fibrinogen assessment might be considered to identify people at higher risk of ICH. As fibrinogen repletion is feasible, trials should investigate its efficacy in preventing ICH, potentially increasing the net benefit profile of IVT in acute ischemic stroke.
PSEUDOXANTHOMA ELASTICUM AND STROKE: A RARE ENTITY

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Background and Aims:: Introduction: Pseudoxanthoma elasticum (PXE) is a rare autosomal recessive connective tissue disease caused by mutations of ABCC6. The deterioration of elastic fibers leads to dermatologic, ophthalmologic, and vascular dysfunction.

Methods:: A woman had 2 episodes of regressive ischemic stroke at the age of 48 and 62 years old respectively. Previously she was a healthy woman, but she had family history of dermatosis and young stroke in first-degree relatives. She developed hypertension by the second ischemic attack. Initial stroke diagnostic protocol, including laboratory studies and cardiac evaluation, was negative. On general examination, she had yellow plaque-like skin lesions on the lateral neck. Ophthalmological exam revealed retinal angioid streaks complicated by neovascularization. Brain MRI and MR angiography revealed multiple lacunar infarcts, with slight focal narrowing of cervical segments of the internal carotid arteries.

Results:: Patients with PXE have higher incidence of ischemic strokes than the general population. Cerebrovascular manifestations include ischemic strokes, transient ischemic attacks and intracranial aneurysms with hemorrhagic strokes. Main mechanisms are early arteriosclerosis and arterial hypertension. Ocular manifestations are retinal pigmentation, angioid streaks and retinal hemorrhages which can lead to blindness. Skin biopsy reveals fragmentation and calcification of elastic fibers. Diagnosis is definite if characteristic skin signs, ophthalmologic and histological features are present.

Conclusions:: PXE must be considered when confronted with ischemic attacks of undetermined origin in young patients. Family history can be useful to suspect PXE. Aspirin should be used with precaution to prevent ocular and neurological thromboembolic events.
RATIONALE FOR INITIATING FEASIBILITY STUDY OF TRIIODOTHYRONINE SUPPLEMENTATION FOR STROKE PATIENTS TO IMPROVE OUTCOMES

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Background and Aims:: According to numerous studies low triiodothyronine (T3) syndrome is associated with poor stroke outcome but possible neuroprotective effects of thyroid hormones are underestimated in human studies. Aim of this study was to determine endogenous thyroid hormones levels effect on stroke outcome.

Methods:: In this study 121 adult patients with first-ever acute ischemic stroke were enrolled. Concentrations of free T3, free T4, TSH and basic stroke risk factors were assessed during 24h from symptoms onset. Neurological deficit was assessed by Scandinavian Stroke Scale (SSS). Patients were dichotomized for mRs 0-2 and 3-6 at 6 months after stroke.

Results:: Patients with fT3 level in 4th quartile (≥5.35 pmol/l) had a less severe deficit (SSS median 48 in Q4 vs. 37 in Q2-3, p=0.0481), especially in compare with Q1 (≤3.4050 pmol/l, SSS median 48 vs. 30, p=0.0018). Patients with free-T3 level in Q4 had a more favorable outcome in comperison with Q2-3 (mRs median 3 (95% CI 2-4 ) vs 4 (95% CI 3-5), overall difference p=0.0175).
Free-T3 level above 8.67 pmol/L was associated with 75% probability of favorable outcome. There was a correlation between fT4 and atrial fibrillation (R=0.297; p=0.0071) but no relationship between thyroid hormones in Q3-4 and increased risk of any cause death or recurrent events.

**Conclusions:** Dose-dependent effects of fT3 on stroke outcome, absence of negative events in high-T3 group and results of previous studies made the rationale of conducting a feasibility trial of T3 supplementation in stroke patients to improve outcomes.
PREDICTION OF EARLY FUNCTIONAL OUTCOMES OF HEMORRHAGIC STROKE

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Background and Aims:: A common limitation of studies on hemorrhagic stroke (HS) outcomes is that authors concentrate exceptionally on clinical data and do not consider environmental factors. There is a rising body of evidence for highly informative value of weather in the forecast. We aimed to predict unfavorable outcomes in patients with HS at the time of discharge from in-patient service in hot dry climate.

Methods:: We studied 160 consequent HS cases admitted over the course of four years. Supervised ML models were built for two classes: mRS ≤ 3 and mRS > 3. To build the models we first performed feature selection. Risk factors were ranked in importance according to their impurity-based predictive potential. To evaluate classifier output quality, we trained models in a stratified 10-fold cross-validation technique.

Results:: The most valuable clinicodemographic factors were BMI, NIHSS at admission and age. The list of significant features predictive of outcome changed pronouncedly when meteorological data was incorporated into the model, in which case NIHSS at admission was the most predictive clinical factor, followed by the changes in air masses during two days preceding the stroke. The inclusion of weather estimates increases the predictive metrics of the classifying model (F1 score of 0.900 vs. 0.667; AUC of 0.896 vs. 0.685).

Conclusions:: Outcomes of HS may be predicted precisely with ML models trained on a combination of the full range of meteorological and clinicodemographic data. Hospitals may improve stroke management practice with the employment of predictive models. Climatic factors should be included in stroke prediction applications.
ATRIAL FIBRILLATION DETECTION IN POST-STROKE PATIENTS: A CLINICAL AUDIT AT PORTIUNCULA HOSPITAL BALLINASLOE.

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Background and Aims: Stroke is a leading cause of death and disability worldwide and approximately 10,000 people have a stroke related event every year in Ireland (1). Atrial fibrillation (AF) is one of the most common sustained arrhythmias and is a major risk factor for stroke (2). However, a substantial number of patients with stroke have asymptomatic AF (3). Thus, the NICE guidelines, recommend that a 24-hour Holter monitor/24-hour ECG monitor be used to detect AF (1). Aims: Identify the number of patients with a background history of AF prior to stroke. In reference to the RCP NICE Stroke guidelines (1), audit if a Holter monitor was performed on all stroke patients without a background of AF.

Methods: A search for all patients who had a stroke between January 2018 and December 2018 in Portiuncula hospital was conducted. Of these 17 patients, 4 patients had a background history of AF prior to their stroke. Abiding by the RCP NICE accredited guidelines 2016, the 13 remaining patients with no background history of AF, should have had Holter monitors performed to assess for undiagnosed AF. The incidence of ischemic stroke increases with age (2). Thus, patients’ ages were also investigated.

Results: 41% of the patients were above the ages of 71 years. 24% of all stroke patients had a background history of AF prior to their stroke.

Conclusions: Stroke patients who have no background of AF and no known cause for their stroke, should have a Holter monitor performed (1).
Background and Aims:: Frailty is an important short and long term predictor of disability in the elderly and might influence the clinical outcome of acute treatment of stroke. Aim of the study was to evaluate whether frailty predicts short- and long term all-cause mortality and neurological recovery in old patients who underwent reperfusion acute treatment of stroke.

Methods:: Consecutive patients older than 65 years who underwent thrombectomy or thrombolysis in a single stroke Unit from 2015 to 2018. Predictors of stroke outcomes were assessed including demographics, baseline NIHSS, time to needle, treatment and medical complications. Premorbid Frailty was assessed with a comprehensive geriatric assessment (CGA). At 3 and 12 months, all-cause death and clinical recovery were evaluated.

Results:: 102 patients, of whom 31 underwent mechanical thrombectomy and 71 venous thrombolysis (mean age 77.5, 65-94 years) entered the study. Frailty was diagnosed in 32 out of 70 patients and associated with older age (p=0.001) but no differences in Baseline NIHSS score or treatment strategies. At follow-up, frail patients showed higher incidence of death at 3 (25% vs 3%, p=0.008) and 12 (38% vs 7%, p=0.001) months. Frailty was the best predictor of worse neurological recovery at 3 month (mRS 3.4 + 1.8 vs 1.9 + 1.9, p=0.005) and one year follow-up (mRS 3.2 + 1.9 vs 1.9 + 1.9) for free survival patients.

Conclusions:: Frailty is an important predictor of efficacy of acute treatment of stroke. Larger longitudinal studies are warranted in order to evaluate the risk-benefit of reperfusion treatment in the growing elderly frail population.
EMBOLIC STROKE COMPLICATION FOLLOWING HEMOPTYSIS EMBOLIZATION: A CASE REPORT

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Background and Aims:: Bronchial and non-bronchial systemic arterial embolization (BAE/ NBSAE) is a safe and effective non-surgical intervention for patients with massive hemoptysis. Stroke is a rare complication of BAE/ NBSAE. We reported a case of cerebellum infarction as a one of complication of BAE/ NBSAE

Methods::

Case: A 33-year-old woman had experienced productive hemoptysis for 3 years. She had a history of completely treated lung tuberculosis, yet she had productive hemoptysis due to cavity with isodens lesion with crescent sign. Both, bronchial and non-bronchial systemic arterial embolization (BAE/NBSAE), had been performed to reduce hemoptysis. The transarterial approach was done accessing right intercostal and intercostobronchial artery. Decannulation of catheter was hard to perform due to tortuous vessels. Unfortunately, the catheter inadvertently engaged to origin of right vertebral artery. It made the suddenly symptoms of vertigo and nystagmus response. The emergency brain non-contrast computed tomography (CT) scan revealed a suspicion of acute infarction of left cerebellum. It was confirmed as an acute infarction of right cerebellum by brain magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA). She then was administered heparin and had completely
neurological recovery for ten days
hospitalization
Results: BAE and NBSAE are effective methods for the control of moderate-massive hemoptysis due to bronchiectasis and pulmonary tuberculosis or aspergilloma. The worldwide prevalence of transient ischemia/stroke and cortical blindness complication following BAE is 0.6-2%. It is mostly attributed to subclavian arteries maneuvers or embolizing agents crossing bronchopulmonary arterial anastomoses. Conclusions: Early detection of neurological dysfunctions following BAE/NBSAE could improve the clinical outcome of neurological complications.
Background and Aims:: Ischemic stroke (IS) in young adults is a serious medical problem due to its potential socio-economic consequences. The risk of recurrence is highest 22% in the first year and 53% in the following five years. Moreover, recurrent stroke is the leading cause of disability and death. Data on long-term survival and recurrence after stroke are missing. We studied temporal trends in 5-year ischemic stroke case fatality and recurrence rates stratified by etiological subtype according to the ORG 10172 trial classification in acute stroke treatment (TOAST).

Methods:: A total of 270 consecutive patients younger than 50 years with a diagnosis of ischemic stroke were included for 5 years in the neurology department. The clinical evaluation consisted of a complete neurological examination and the National Institutes of Health Stroke Scale. Diagnostic workup included vascular axis exploration, extensive laboratory, radiological, and cardiological examination. Etiology-specific time trends for recurrence were estimated by Cox regression.

Results:: The mean age of the patients was 41 ± 7 years and the sex ratio was 1. Recurrence of IS was noted in 98 patients. According to TOAST classification, atherosclerosis and cardio-embolism were associated with stroke recurrence in our study. Moreover, the hazard ratio (HR) of determinate causes of stroke was 3.658 (95% CI 1.837-7.284) dominated by hypercoagulability state. Thrombophilia was associated with recurrence vascular accident (p:0.001), the HR was 2.293 (95%CI 1.405-3.741).

Conclusions:: Thrombophilia increases the risk of early recurrent IS in young adults. They require special secondary prevention efforts.
SPEECH AND NEUROPSYCHOLOGICAL STATUS IN A RUSSIAN-LANGUAGE PATIENT WITH CROSSED APHASIA: A CASE STUDY

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Background and Aims:: Clinical cases of crossed aphasia in Russian-speaking patients, especially in ambidextrous, have not yet been adequately described. In the current study, we report a patient (male, 49 years old, Russian monolingual, ambidextrous: right-handed in writing, left-handed in everyday activities) with aphasia and neuropsychological deficits after right hemisphere (RH) hemorrhagic stroke.

Methods:: MRI of the brain; EEG-monitoring; neurological examination; neuropsychological (A.R.Luria's methodology) and speech (methodology of T.V.Akhutina, L.S.Tsvetkova, N.M.Pylaeva) assessment.

Results:: In September, 2020, a patient had a stroke – putamenal hemorrhage in RH with the development of left-sided hemiparesis to plegia in the arm, left-sided hemihypesthesia, left-sided homonymous hemianopsia. MRI: acute hemorrhage in the RH of the brain, putamenal region. EEG-monitoring: interhemispheric asymmetry, continued deceleration of background activity to the theta range in RH with regional deceleration to the delta range in the temporo-central parietal area. The patient passed through endoscopic removal of hypertensive right-sided putamenal hematoma using neuronavigation. Speech and neuropsychological assessment: complex cross aphasia (efferent motor and semantic according to A.R.Luria’s classification, severe prosodic violations); severe acalculia, dysgraphia, moderate dyslexia; premotor apraxia followed by a moderate deficit in the executive functions; left-sided neglect due to hemianopsia.

Conclusions:: The current study represented symptoms of speech disorders in ambidextrous patient with aphasia which are typical for the dominant left hemisphere damage in right-handed patients and a range of deficits (severe prosodic violations) which are typical for the dominant RH damage in right-handed patients. This work was supported by the Program of Strategic Academic Leadership of Kazan Federal University.
NEURON-SPECIFIC ENOLASE AS A BIOMARKER OF ISCHEMIC STROKE

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Background and Aims:: Early detection and evaluation of ischemic stroke (IS) can have a positive impact on its outcomes. One of the most promising ways is to use neuron-specific enolase (NSE). The goal of this study was to clarify the serum levels of NSE in the acute period of the IS and define their relationships with severity of neurologic deficit and short-term outcomes.

Methods:: 63 patients with IS and 20 controls were included in this study. Blood samples were drawn in the first 72 hours (point 1, p1) and 10-14 days (point 2, p2) since the IS, once in controls. Severity of neurological deficit, short-term outcome and functional outcome were evaluated with NIHSS, Rankin (mRs), Rivermead and Barthel scales twice at p1 and p2.

Results:: NSE levels were elevated in 66.6% of patients with IS at p1, which was significantly different from controls (29.3±3.9 and 15.5±1.4, p=0.002), lowering significantly by p2 (17.5±0.9; p = 0.003). In patients with the higher severity at p1 NSE at p1 was higher (p=0.03), and with higher severity in p2 NSE were higher at p1 (p=0.04) and p2 (p=0.005). Correlations were found between NSE at p1 and Barthel at p2 (r=0.3) and Rivermead at p2 (r=0.27); NSE at p2 and NIHSS at p1 (r=0.31) and p2 (r=0.28), mRs at p1 (r=0.34) and p2 (0.26), Barthel at p1 (r=-0.3) and p2 (r=-0.34), Rivermead at p1 (r=-0.35) and p2 (r=-0.33).

Conclusions:: NSE can be useful for stroke diagnostics, prognosis, monitoring and estimating rehabilitation potential in the acute period of the ischemic stroke.
SUCCESS AND PITFALL OF ANTICLOTTING THERAPY

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Background and Aims:: In Italy, prescription of novel therapeutical agents is under strict control. Nonetheless, efficacy and safety of NOACs (Novel Anti-Clotting drugs) fostered their off-label prescription.

Methods:: We recruited the following patients affected with atrial fibrillation (AF): 7 Chronic Cerebrovascular Disease (CCVD), 58 Acute Stroke (AS), treated with NOAC; 13 CCVD and 98 AS, under Vitamin K Anticoagulants (VKA). INR of the latter at emergency department was < 2 in 40 (52%), > 3 in 15 (19%), 2-3 in 22 (29%) AS patients.

Results:: Rivaroxaban, apixaban, edoxaban and dabigatran were prescribed in 30 (45%), 18 (27%), 10 (15%) and 8 (12%) patients, respectively. According to pharmaceutical recommendations, under dose or upper dose were reported in a minority of patients. However, the prescription resulted to be “inappropriate” considering valvular cardiopathy at echocardiography. No NOAC treated patients had haemorrhagic infarction. Among VKA treated AS patients, aortic and mitralic prosthesis, moderate-severe mitral, aortic and tricuspidal failure, septal aneurisms, dilatative chronic ischaemic cardiomyopathy were present. Haemorrhagic infarctions occurred in 10/77 (13%) AS patients (4 in INR < 2, 3 in INR 2-3, 3 in INR > 3).

Conclusions:: Our results confirm the safety of NOAC. Their efficacy may be lessened in moderate-severe valvulopathies. Further studies are needed in order to validate the probable reduction in mortality. The paradox of no differences in the rate of haemorrhagic infarction related to the entity of anticlotting effect of VKA, in the absence of traumatic events, highlight the increased risk related to underlying cardiological dysfunction and late recanalization.
PREVALENCE OF ASYMPTOMATIC UNRUPTURED INTRACRANIAL ANEURYSM IN THE ELDERLY THAI POPULATION

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Background and Aims:: Subarachnoid hemorrhage is one of the devastating cerebrovascular event. Ruptured intracranial aneurysm is the leading cause of subarachnoid hemorrhage. Early detection of unruptured intracranial aneurysm (UIA) may help prevent subarachnoid hemorrhage. This study aimed to identify the prevalence of asymptomatic UIA among elderly Thai population.

Methods:: Participants age ≥ 55 years old who had no previous history of ischemic or hemorrhagic stroke were enrolled in the study. Magnetic Resonance Imaging with MR angiography were performed in all participants. Aneurysms types, sizes, and locations were evaluated. Baseline characteristics among participants with and without saccular aneurysms were compared.

Results:: Two hundred participants were enrolled in the study, 136 (68%) were female. Twenty-six aneurysms were detected in 22 participants. Among these, 20 participants (90%) and 2 participants (10%) had saccular and fusiform aneurysm respectively. Prevalence of unruptured intracranial saccular aneurysm was 10%. Mean (SD) size of saccular aneurysms was 3.05 (1.71) mm. (max 10 mm., min 1.2 mm.). Cavernous part of internal carotid artery (ICA) was the most common location of saccular UIA (33%) followed by supracinoid (25%) and paracintoid (25%) ICA. There was non-significant trend towards higher female and smoking participants with saccular UIA. Other risk factors including age, smoking, diabetes mellitus, hypertension, dyslipidemia, and peripheral arterial disease were similar between 2 groups. None of the participants had subarachnoid hemorrhage during 6 months follow-up period.

Conclusions:: This is the first study to demonstrate the prevalence of UIA among elderly Thai population without previous history of stroke.
EPISODES OF PULSELESS, NON-PERFUSING RHYTHM: A SUBTLE KILLER

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**Background and Aims:** Cardiovascular reactivity (CR) may be defined by beat indices (ratio or difference) between higher maximal or minimal heart rate (HR) on higher maximal or minimal pulse rate (PR) (Fiori P. et al., 2020). Episodes of negative CR (NCR) may subtly occur and impair cerebrovascular and cardiovascular function. The aim of our study was to examine the correlation between haematological parameters (HP), Holter Arterial Pressure Measurements (HAP) and burden of vascular encephalopathy (VE) in acute ischaemic cerebrovascular events, chronic cerebrovascular diseases (CCVD), other neuropsychiatric disorders (OND).

**Methods:** VE was calculated by scoring the presence of: - enlarged liquoral space (1); - white matter hyperintensities (1); - lacunar Acute Stroke (AS) (1); - AS > 0.5 cm diameter (2); - enlarged perivascular space (1); - cerebral microbleeds (1).

**Results:** Significant differences and correlations were found concerning HP, HAP and outcomes in AS, CCVD compared to OND. VE was found in 29% OND, 100% CCVD, 84% AS. Patients with NCR have a higher probability of AS and/or CCVD (AS OR 4, CCVD OR 6).

**Conclusions:** CR correlates with VE. Anti-hypertensive therapies may account for discrepancies in CR in CCVD. Three stages of ischaemic lesional burden may be conceived: I - Preserved ejection fraction (prEF), high CR / low VE risk; II - PrEF, low CR / intermediate VE risk; III - Reduced EF, low CR / high VE risk (no-perfusion, core, no-collateral compensation). The relation of HR, PR with age and VE may be represented by U and reversed U curves, respectively.
FOCUSING ON SINGLE CT PERFUSION QUANTITATIVE MAPS: PERCHERON’S ARTERY STROKE DETECTION IN AN EMERGENCY SETTING

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Background and Aims:: Occlusion of Percheron Artery may be challenging due to its rare occurrence, confounding clinical presentation and neuroimaging assessment.

Methods:: Here we report the case of a 58-years-old man admitted to the Stroke Unit after awakening with drowsiness, global aphasia, right hemiplegia symptoms (NIHSS=19), a Total Anterior Circulation Syndrome mimicking an infarct in the territory of the middle cerebral artery.

Results:: Non-Enhanced Computed Tomography (NECT), CT angiography and CT Perfusion (CTP) core/penumbra summary map did not show abnormalities. Follow-up NECT at 24 h showed bilateral thalamic hypodensity. Because of the late presentation the patient was not treated with thrombolysis and died six days later. Despite the initial CTP core/penumbra summary map was negative, the careful re-evaluation of single parametric CTP maps (MTT/TTP/CBF/CBV) revealed bilateral symmetrical thalamic hypoperfusion in TTP, CBF and MTT, but no CBV alteration, a suggestive pattern of penumbra in the Percheron’s artery territory(Figure 1). This symmetrical alteration of parametric maps yields a negative core/penumbra summary map if the software criteria is based only on the asymmetry-based thresholds, so the median vascular territories are not visualized on the summary map.

Conclusions:: In conclusion, this case highlights the opportunity of early diagnosis of Percheron’s artery occlusion through complete CTP analysis, which require both the acknowledgment of the automatic core/penumbra summary maps’ pitfalls and the evaluation of all parametric maps.

Figure 1. (A) NECT at admission; (B) CTP core/penumbra summary map; (C), (D), (E), (F) Quantitative CTP parameters maps - MTT, CBV, TTP, CBF, respectively. Single CTP quantitative maps revealed bilateral symmetrical thalamic marked hypoperfusion in TTP, CBF and MTT; (G) follow-up NECT.
Background and Aims: To analyze modern approaches to the treatment of speech disorders in patients with acute ischemic stroke.

Methods: A total of 115 people with ischemic stroke was examined. Patients were divided into three groups: 35 with aphasia, 42 with dysarthria and 38 patients without speech disorders. Rivermid mobility index, the MMSE, the Hamilton scale and the aphasic test were applied.

Results: In the first group the average on the Hamilton scale was 10.2 points, 16.4 points on the MMSE, and the Rivermid index was 4.6. A strong correlation of $r = 0.67$ was found between the motor disorders and depressive manifestations. Applying the Hamilton scale was difficult for this group, but indirect signs of depression were common - 83%. In a group of patients with dysarthria: the mean value on the Hamilton scale of 9.7 and the index of motor disorders of 4.3; also indirect signs of depressive manifestations (36%) were found. In this group, there was a strong correlation ($r = 0.78$) between the indicators of mobility index and the presence of depression on the Hamilton scale. In the group without speech disorders, the medium value for the depression scale was 9.1 points, the cognitive impairment on the MMSE was 20.2 points, and the Rivermid index - 4.8 points. Indirect signs of depression - 20%.

Conclusions: The high prevalence of clinically significant depressive manifestations among the patients with speech disorders was found.
WRONG OR RIGHT DECISION MAKING?

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Background and Aims:: High density of population, lack of birth control in developing countries with subsequent emigration, extreme social and economic differences, poor environmental resources, conflicts are emerging challenges to political and economic assets all over the world

Methods:: A 28 years-old, Nigerian, male patient was transferred to our Neurological Unit from First Aid for subacute, ischaemic stroke caused by a large occlusion of right, middle cerebral artery. He came to observation because of cephalalgia, agitation, left facio-brachio-crural hemiparesis with hypoesthesis, sphincterial release, tachycardia, pulmonary crackling.

Results:: Assay for psychotropic substances showed tetrahydrocannabinoid positivity. A wide, right fronto-parieto-temporal ischaemia, pleural effusion, dilatative cardiomyopathy were present at Computerized Tomography. Thoracic Echocardiography detected a thromboembolic formation in left ventricle and an ejection fraction of 20%. At admission, the following parameters were revealed: arterial pressure 122/85 mmHg, heart rate 56 b/min, respiratory rate 22, body temperature 36.3°C, SaO2 70%, NIHSS 23. Haematological examinations showed monocytosis, increased Erythrosedimentation Rate, C-Reactive Protein, hsTroponin, Brain Natriuretic Peptide, d-dimer, a1, a2 proteins, decreased albuminemia, g globulins, presence of albuminuria, anti-HCV, anti-rubeola, anti-EBNA, anti-cytomegalovirus IgG positivity. Titer of anti-Lupus Anticoagulant antibodies was high. Asymptomatic stenosis of left internal carotid artery was revealed by EchoDoppler Ultrasonography. A diagnosis of cardioembolic ischaemic stroke, dilatative cardiomyopathy, suspected post-infectious vasculitis was posed. Because of incipient heart failure, a defibrillator was implanted. The patient was transferred to rehabilitation for further diagnostic analyses and physio-kinesis-therapy.

Conclusions:: A concerted action is needed in order to establish a common strategy for ensuring humanitarian, medical assistance, safeguarding shared rules and public health care.
Background and Aims:: Hypereosinophilic syndrome (HES) is a rare cause of recurrent ischemic stroke and the underlying pathogenesis is heterogeneous. Herein, we describe a gentleman presenting with recurrent strokes due to idiopathic HES for 3 years, with a dramatic response to Imatinib.

Methods:: A 56-year-old gentleman with dyslipidemia, hypertension and past history of multiple strokes involving different vascular territories presented with acute onset slurring of speech and left sided weakness. Neurological evaluation showed dysarthria and left hemiparesis. He also complained of dry cough for 6 months and non-specific symptoms like fatigue, myalgia. His investigations (Figure 1 and Table 1) confirmed the HES and Hydroxyurea and Prednisolone was started. Imatinib was started after 6 months due to poor response and the eosinophil count normalized within 3 months.

Figure 1: (A) sagittal, (B, C) axial T1 flare and (D) DWI brain images showing multiple acute infarcts in right side with bilateral multiple chronic lacunar infarcts and evidence of small vessel disease.
Results: HES is diagnosed based on persistent eosinophilia (≥ 1500 eosinophils/mm³) for at least 6 months, organ involvement including cardiac, brain, bone marrow and exclusion of other conditions. The treatment goal is to reduce the eosinophil level in blood and tissues to prevent tissue damage. Treatment includes glucocorticoids, hydroxyurea, Chlorambucil and Vincristine. Tyrosine kinase inhibitors such as Imatinib indicated for patients with positive FIP1L1-PDGFRA fusion. Mepolizumab (antiIL-5) has received FDA approval recently for negative FIP1L1-PDGFRA. Our patient was treated with Imatinib even though his mutation was negative and he responded excellently.

Conclusions: HES is a treatable cause of recurrent stroke and need to consider particularly when involving different vascular territories. HES can be fatal, hence early diagnosis and prompt treatment to mitigate disability and mortality is essential.

<table>
<thead>
<tr>
<th>Table 1: Investigations</th>
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<tr>
<td>Lipid profile</td>
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<tr>
<td>Electrocardiogram</td>
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<tr>
<td>Carotid doppler</td>
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<td>Transthoracic echocardiogram (TTE)</td>
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<td>Transesophageal echocardiogram (TOE)</td>
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<td>Thrombophilia profile</td>
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<tr>
<td>Autoantibodies</td>
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<tr>
<td>Serum Homocysteine</td>
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<td>FBC</td>
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<tr>
<td>Stool examination</td>
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<td>Serum creatinine</td>
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<td>Urine routine examination</td>
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<td>Genetic testing</td>
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<td>Bone marrow</td>
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PROTEIN S DEFICIENCY AND MTHFR MUTATION: AN UNCOMMON CAUSE OF SPINAL CORD INFARCTION: A CASE REPORT

Nesrine Charfi1, Ines Bedoui2, Bissene Douma2, Hajer Derbali3, Malek Mansour4, Ridha Mrissa4
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Background and Aims:: Ischemia of the spinal cord represents only 5 to 8 % of acute myelopathies and < 1% of all strokes. The clinical and radiological presentation are varied. Protein S deficiency and MTHFR mutation are an uncommon cause of spinal cord infarction and often misdiagnosed. Aim : To recommend an exhaustive etiological assessment in front of any spine ischemia in young adult.

Methods:: This is a case about a patient who was diagnosed with spinal cord infarction due to protein S deficiency at the primary military hospital of Tunis.

Results:: A 27-year-old pregnant women, presented with acute onset of flaccid quadriplegia associated with bladder incontinence. On initial examination she was afebrile. Muscle strength was 0 out of 5 in bilateral upper and lower extremities, with generalized loss of tone. Muscle stretch reflexes were absent. Sensory evaluation revealed absent sensation to all modalities with a C4 sensory level. Repeat spine Magnetic resonance imaging (MRI) showed central cord T2 hyper intensity C4-T2, with prominent owl sign on transverse views. An exhaustive etiological assessment including cérebro spinal fluid analysis, cardiac exploration, and laboratory panels found a protein S deficiency and MTHFR mutation. Patient was treated with aspirine and outcome was favorable.

Conclusions:: Unlike the classical etiologies of spinal cord ischemia, haematological cause, in particular the protein S deficiency and MTHFR mutation must be researched in young adults.
CEREBRAL AIR EMBOLISM: A HIDDEN CAUSE OF ACUTE ISCHEMIC STROKE.

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Background and Aims:: Cerebral air embolism (CAE) is a rare but well-documented complication of endoscopic procedures. The precise mechanism is still debatable since no right-to-left shunts are found in most cases.

Methods:: Case-report

Results:: A 46-year-old male with a history of eosinophilic oesophagitis presented to the Emergency Department because of food bolus impaction. Under general anesthesia, an emergent EGD was performed and the bolus was successfully pushed into the stomach. Three hours later the patient complained of drowsiness and left-sided weakness. Brain CT-scan was unremarkable. Neurologic examination revealed left-sided sensory-motor impairment and hemianopia. Intravenous thrombolysis was started and the patient was referred to our tertiary center for stroke treatment. CT-angiography failed to prove large vessel occlusions but revealed a pneumo-mediastinum (FigureA). A second EGD confirmed a small oesophageal laceration without signs of perforation or bleeding (FigureB). Follow-up brain MRI revealed two ischemic lesions in the right hemisphere, in both anterior and posterior territories (FigureC-D). Echocardiography and prolonged cardiac monitoring resulted normal. Transcranial doppler with bubble test was unremarkable. A presumptive diagnosis of CAE was made. A definite diagnosis must be supported by a brain CT-scan positive for air detection. However, air dissolves quickly in the blood and in most reported cases no evidence of air embolisms can be demonstrated with CT-scan already after few hours from the acute event.
Conclusions:: Despite its rarity, cerebral air embolism should be considered when neurologic impairment occurs soon after endoscopic procedures, in order to promptly implement the correct treatment (e.g. hyperbaric chamber) and to avoid potentially catastrophic consequences from misdiagnosis.
THROMBECTOMY FOR ISCHEMIC STROKE WITH LARGE VESSEL OCCLUSION AND CONCOMITANT SUBARACHNOID HEMORRHAGE

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Background and Aims:: Nontraumatic subarachnoid hemorrhage (SAH) can rarely occur in the acute phase of ischemic stroke (AIS), especially if due to large vessels occlusion (LVO). Such intracranial bleeding hinders AIS management and the choice of revascularization approach.

Methods:: Case report.

Results:: A 52 year-old man presented with acute right hemiparesis and aphasia. Brain CT showed a SAH in the left central sulcus (Fig. 1A). CT-angiography revealed sub-occlusive stenosis of the left internal carotid artery (ICA, Fig. 1B) and the occlusion of the left middle cerebral artery (MCA, Fig. 1C). The patient underwent an emergent angiographic procedure with successful recanalization (TICI score of 3). Follow-up CT, 24 hours later, demonstrated an ischemic lesion in the striatal-lenticular region (Fig. 2B) without SAH progression.
While the absolute contraindication to IVT during intracranial bleeding remains unquestionable, the potential injury/benefit from MT is still debatable. Thus, cases like ours constitute a blind spot in the guidelines where physicians face the dilemma of choosing between an acute endovascular treatment with the risks of hemorrhage progression and conservative treatment with the associated poor clinical outcome. We decided to treat our patient invasively, considering the relatively young age and the expected poor clinical outcome following untreated tandem occlusion, also given the absence of prognostic factors that generally predict post-procedural reperfusion injury (hyperglycemia, low ASPECTS, hypertension, older age, delayed onset-to-treatment time, high NIHSS etc.).

**Conclusions:** We believe that, in similar cases, MT should be considered – despite not free of risks and drawbacks – to avoid the detrimental consequences of untreated AIS from LVO.
MIMICS AND CHAMELEONS IN THE REPERFUSION ERA: TWO CASE REPORTS

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ASL TO 4 Cirié Hospital, Neurology, Cirié, Italy

Background and Aims:: Stroke mimics and chamaleons cannot always be ruled out in emergency and we have to manage the risk of misdiagnosis to properly treat our patients.

Methods:: We describe two cases occurred in our emergency department (ED).

Results:: A 84 years old woman presented to ED at 2 p.m. because of acute nonfluent aphasia, last time seen well at 9 a.m. TC scan was normal and ischemic stroke was suspected. Neither thrombolysis (onset>4,5 hours) nor thrombectomy (no artery occlusion demonstrated) were performed. She recovered spontaneously in 24 hours. An EEG documented lateralized periodic discharges on left hemisphere and MRI revealed left mesial temporal and pulvinar hyperintensity on T2 and DWI; CSF examination excluded encephalitis and aphas； Status epilepticus was diagnosed. A 86 years old man, on DOACs for atrial fibrillation and previous stroke, referred to ED because of sudden loss of consciousness with diffuse rigidity. On examination one hour after onset, the patient was alert with speech impairment and right paresis. TC scan demonstrated old ischemic lesions and seizure due to remote stroke with post ictal deficits was suspected. 24 hours later symptoms were persistent with a left medial talamic ischemic lesion on TC scan according to top of basilar syndrome.

Conclusions:: In ED we need to go fast and accept the risk of treating a few mimics; the problem with chamaleons is more serious because unrecognized stroke means a patient not properly treated.
ISCHAEMIC STROKE AFTER SNAKEBITE: A CHALLENGING DIAGNOSIS AND TREATMENT

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Background and Aims:: Introduction: Snakebite envenoming represents a common cause of morbidity and mortality in developing countries, whereas it is a more unusual event in Europe, affecting 0.4 to 1.1 people per 100,000 population per year and causing approximately 1000 severe envenoming cases and less than 5 deaths per year. Post-snake envenomation stroke (both ischaemic and hemorrhagic) pathogenesis is multifactorial, depending on several mechanisms such as vascular endothelial damage and blood coagulation impairment. To our knowledge, only one case of hemorrhagic stroke has been described in Europe, while no cases of ischaemic stroke have been reported so far.

Methods:: Not available

Results:: Case presentation: A 66-year old man was admitted to our Emergency Department complaining diplopia and postural instability 24 hours after a viper bite on his left foot. Magnetic Resonance Imaging showed multiple bilateral ischaemic lesions involving anterior and posterior circulation, without arterial stenosis or occlusion. Muscle and cardiac venom damage was also present.

Conclusions:: We present the case of a patient who suffered from an ischaemic stroke with an embolic pattern after viper bite in Rome surrounding. Although the low frequency of snake bites at our latitudes, viper envenomation can cause severe complications and must be recognized and promptly treated. Neurologists need to be aware that viper envenomming can also be a possible rare cause of stroke and antivenom should be promptly administered to avoid this complication. Indeed, the high risk of serious events in symptomatic victims is much greater than the low risk of anaphylaxis associated with high quality modern antivenoms.
CEREBRAL VENOUS THROMBOSIS POST LOBAR PUNCTURE

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CHU Sétif service neurologie, Neurology, SETIF, Algeria

**Background and Aims::** Cerebral venous thrombosis (CVT) is a multifactorial disease which can result from the association of several risk factors. Lumbar puncture (LP) and epidural anesthesia could be the cause of TVC but no study formally shows their involvement in the occurrence of this pathology.

**Methods::** Observation We report 03 cases (02 women and 01 man). During a lumbar puncture in the context of exploring cerebral demyelinating pathology, the 2 patients aged 27 and 32 respectively presented abnormally intense headaches, not responding to the usual analgesics and the patient aged 39 years of age presented with complex focal motor epileptic seizures. The performance of angio-MRI confirmed the presence of TVC in these patients.

**Results::** Lumbar puncture is frequently performed as part of the exploration of neurological pathologies. Post-lumbar puncture syndrome is common, found in 12 to 38% of cases depending on the series. A link between PL followed by intravenous steroid treatment is suspected to be the cause of the occurrence of CVT, with or without risk factors such as thrombophilia. It is difficult to assess the part of the responsibility of LP in the occurrence of CVT because it is often carried out during the exploration of pathologies themselves at risk of thrombosis.

**Conclusions::** It appears that in the course of LP, the presence of post-LP syndrome prolonged beyond the usual times with or without epileptic seizure, should suggest a CVT. The precocity of diagnosis thanks to cerebral angio-MRI and the speed of initiation of an anticoagulation condition the prognosis.
Safflower yellow (SY) inhibits the ischemia and hypoxia-induced inflammatory signaling transduction in both rats and BV2 cell lines

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Background and Aims:: Ischemia and hypoxia may induce inflammation in CNS. Our aim was to investigate the effects of Safflower Yellow (SY), the main active component in the traditional Chinese medicine safflower, on the ischemia and hypoxia-induced inflammatory signal transduction in both rats and BV2 cell lines.

Methods:: SD rats were randomly divided into 3 groups: control, tMCAO model and SY-treated group. The neurological deficits of rats were evaluated. The rats were sacrificed for the following assessments, including TTC staining, HE staining and RT-PCR and Western Blot. BV2 cells were divided into 3 groups: control, OGD/R and SY-treated group and assessed by RT–PCR, Western Blot and ELISA.

Results:: Compared with the control group, the behavioral function in tMCAO group was declined, while the SY application could ameliorate the changes. SY treatment significantly decreased the brain infarct volume and alleviated the pathological impairment. Compared with the control group, cell viability in OGD/R BV2 group was decreased, while SY treatment obviously improved the viability. SY suppressed the elevation of both mRNA and protein of TLR-4, TNF-α and IL-6 in tMCAO rats and OGD/R BV2 cells. Meanwhile, we found SY treatment decreased NF-κB p65 in tMCAO rats and OGD/R BV2 cells.

Conclusions:: SY effectively inhibits the ischemia and hypoxia-induced inflammatory signaling transduction in rats and BV2 cell lines. (NSF of China, 82004028; Fellowship of China Postdoctoral Science Foundation, 2020M680912; Shanxi Applied Basic Research Project, 201901D211538; Young Scientists Cultivation Project of Shanxi University of TCM,2021PY-QN-09,Ma and Huang are corresponding authors.)
Background and Aims: In recent decades, a detailed picture of language lateralization (LL) has emerged: LL can differ across the sub-processes (speech production, speech perception, and reading) and individuals (Haegen & Cai, 2019). The present study seeks to find lesion data to reflect on the gradient notion of LL.


Results: SE, a 69-year-old female had a sudden onset of aphasia and left hemiplegia. Neuroimaging studies of her brain revealed a hemorrhagic lesion in the right head of the caudate and putamen (See Figure 1.). Her language was categorized as global aphasia in the first week after onset. Seven weeks post-onset, her aphasia syndrome evolved into agrammatic Broca’s aphasia. At this stage, symptoms of speech apraxia and limb apraxia have persisted. Her LVF neglect also persisted. TS, a 76-year-old female suffered a stroke that had resulted in global aphasia and left-sided weakness. Brain imaging revealed large lesions in the areas of right temporal, parietal and frontal areas (See Figure 2.). Severe impairment of all language sub-processes persisted at 19 months post-onset. A systematic review of crossed aphasia in 38 published articles revealed the occurrence of all syndromes of aphasia that are usually reported in left hemisphere damage (See Table 1.).

Conclusions: The findings of the present study appear to offer support for the gradient view of LL.
INTERNETABLE MACHINE LEARNING FOR EARLY NEUROLOGICAL DETERIORATION PREDICTION IN ATRIAL FIBRILLATION-RELATED STROKE

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Background and Aims:: We aimed to develop a novel prediction model for early neurological deterioration(END) based on an interpretable machine learning(ML) algorithm for atrial fibrillation(AF)-related stroke and to evaluate the prediction accuracy and feature importance of ML models.

Methods:: Data from multi-center prospective stroke registries in South Korea were collected. After stepwise data preprocessing, We utilized logistic regression, random forest, extreme gradient boosting, support vector machine, light gradient boosting machine (LightGBM), and Multilayer perceptron models. We then used the Shapley additive explanations (SHAP) method to evaluate feature importance.

Results::

<table>
<thead>
<tr>
<th>Model</th>
<th>AUC [95% CI]</th>
<th>Brier Score</th>
<th>vs Logistic Regression</th>
</tr>
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<tbody>
<tr>
<td>Logistic Regression</td>
<td>0.701 [0.647-759]</td>
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<tr>
<td>Support vector machine</td>
<td>0.723 [0.668-777]</td>
<td>0.109</td>
<td>0.436</td>
</tr>
<tr>
<td>XGBoost</td>
<td>0.771[0.722-0.819]</td>
<td>0.105</td>
<td>0.011</td>
</tr>
<tr>
<td>Light GBM</td>
<td>0.778[0.726-0.830]</td>
<td>0.102</td>
<td>0.005</td>
</tr>
<tr>
<td>Multi-layer perceptron</td>
<td>0.767[0.713-0.820]</td>
<td>0.103</td>
<td>0.002</td>
</tr>
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</table>

Matrix plots of top 24 important features. Bar plot (A) and violin plot (B).
Of the 3,623 stroke patients, the 2,363 who had arrived at the hospital within 24 hours of symptom onset and had available information regarding END were included. Of these, 318 (13.5%) had END. The LightGBM model showed the highest area under the curve (0.778, 95% CI, 0.726 - 0.830). The feature importance analysis revealed that the National Institute of Health Stroke Scale score and fasting glucose were the most influential factors.

Conclusions: The LightGBM model was particularly useful for predicting END. The SHAP method can be adjusted to individualize the features’ effects on the predictive power of the model.
INVOLVEMENT OF POLYMORPHISMS OF COMPLEMENT LECTIN PATHWAY SERINE PROTEASES ENCODING GENES IN ETIOPATHOGENESIS OF ISCHEMIC STROKE

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Background and Aims:: Complement is a major part of innate immune system. The complement system is a proteolytic cascade, where serine proteases activate each other by limited proteolysis in a strictly ordered manner. Serine proteases are essential in both the initiation and the amplification of the cascade. The aim of current study was to reveal the possible involvement of complement lectin pathway mannan-binding lectin-associated serine proteases, MASP-1 and MASP-2 in etiopathogenesis of ischemic stroke (IS) by investigating the potential association of single nucleotide polymorphisms (SNPs) in their genes (rs3203210, rs28945070, rs28945073 in MASP1 gene and rs2273343, rs12711521, rs147270785 in MASP2 gene) with IS.

Methods:: 250 IS patients and 300 healthy subjects were genotyped using the method of SSP-PCR. All primers were designed using the genomic reference sequences of studied genes. The presence/absence of allele-specific amplicons in the genotyping products was visualized by ethidium bromide stained 2% agarose gel. The significance of differences in genotype and allele frequencies and minor allele carriage between patients and HS was determined using Pearson's Chi-square test. The odds ratio (OR), 95% confidence interval and Pearson's p-value were calculated to evaluate the effects of any difference.

Results::

![Diagram of MASP1 and MASP2 genes with SNPs](image-url)
The genotype distribution was in correspondence with Hardy-Weinberg equilibrium in both groups. The results of genotyping demonstrated association of two SNPs (rs3203210 in MASP1 gene and rs147270785 in MASP2 gene) with IS.

**Conclusions:** MASP1 rs3203210 and MASP2 rs147270785 SNPs are strongly associated with IS, and their rs3203210*C and rs147270785*A minor alleles may be considered as protective factors for IS at least in the Armenian population.

<table>
<thead>
<tr>
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<th>IS (Freq.)</th>
<th>HS (Freq.)</th>
<th>P</th>
<th>OR</th>
<th>95% CI</th>
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<td>Genotypes (Freq.)</td>
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<tr>
<td>GG</td>
<td>91 (0.46)</td>
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<td>72 (0.29)</td>
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<td>G</td>
<td>261 (0.65)</td>
<td>241 (0.48)</td>
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<td>&lt; 0.0001</td>
<td>0.496</td>
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<td>115 (0.46)</td>
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<td>G</td>
<td>186 (0.49)</td>
<td>216 (0.43)</td>
<td>= 0.02</td>
<td>0.733</td>
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<td>G</td>
<td>144 (0.72)</td>
<td>165 (0.66)</td>
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<td>1.325</td>
<td>0.884 - 1.985</td>
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<td>35 (0.14)</td>
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<td>89 (0.45)</td>
<td>121 (0.49)</td>
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<td>94 (0.38)</td>
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<tr>
<td>C</td>
<td>183 (0.46)</td>
<td>191 (0.38)</td>
<td>= 0.32</td>
<td>0.753</td>
<td>0.561 - 0.987</td>
</tr>
<tr>
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<td>209 (0.53)</td>
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<td>T</td>
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<td>215 (0.86)</td>
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<td>0.53</td>
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<td>66 (0.26)</td>
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<tr>
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<td>276 (0.68)</td>
<td>244 (0.49)</td>
<td>&lt; 0.0001</td>
<td>0.489</td>
<td>0.349 - 0.693</td>
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<tr>
<td>A</td>
<td>136 (0.33)</td>
<td>256 (0.51)</td>
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<td>Minor allele carriage (Freq.)</td>
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<td>190 (0.76)</td>
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<td>AA</td>
<td>79 (0.40)</td>
<td>86 (0.34)</td>
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<tr>
<td>AG</td>
<td>95 (0.48)</td>
<td>109 (0.44)</td>
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<tr>
<td>GG</td>
<td>26 (0.13)</td>
<td>55 (0.22)</td>
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<td>G</td>
<td>253 (0.63)</td>
<td>281 (0.56)</td>
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<td>A</td>
<td>147 (0.37)</td>
<td>219 (0.44)</td>
<td>= 0.03</td>
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<td>0.57 - 0.976</td>
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<td>164 (0.66)</td>
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<td>29 (0.15)</td>
<td>30 (0.12)</td>
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<tr>
<td>CA</td>
<td>80 (0.40)</td>
<td>97 (0.39)</td>
<td></td>
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<tr>
<td>AA</td>
<td>91 (0.46)</td>
<td>123 (0.49)</td>
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<tr>
<td>C</td>
<td>138 (0.35)</td>
<td>157 (0.31)</td>
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<tr>
<td>Alleles (Freq.)</td>
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<tr>
<td>A</td>
<td>256 (0.66)</td>
<td>344 (0.59)</td>
<td>= 0.22</td>
<td>0.859</td>
<td>0.653 - 1.148</td>
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<tr>
<td>A</td>
<td>171 (0.86)</td>
<td>220 (0.88)</td>
<td>= 0.43</td>
<td>0.804</td>
<td>0.465 - 1.391</td>
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NEUROAID USE IN INTRACRANIAL HEMORRHAGE (ICH)

Ramesh Kumar¹, Farizal Fadzil², Soon Bee², Palani Kamalanathan², Ainul Jaffar², Sanmugarajah Paramasvaran², Toh Jeng², Jegan Thanabalan², Azizi Bakar², Peh Shawn²  
¹University Kebangsaan Malaysia Medical Centre, Division Of Neurosurgery, Department Of Surgery, Kuala Lumpur, Malaysia, ²University Kebangsaan Malaysia, Division Of Neurosurgery, Department Of Surgery, Kuala Lumpur, Malaysia

Background and Aims: MLC601/MLC901 (NeuroAiD™), a combination of natural products, has been shown to be safe and to aid neurological recovery after brain injuries, particularly ischemic stroke. Few studies explored NeuroAiD use in primary intracerebral hemorrhage (ICH). The NeuroAiD Safe Treatment Registry (NeST) studies NeuroAiD use in the real-world setting. This cohort study aimed to assess its use and safety in ICH.

Methods: The online NeST registry of subjects with ICH given NeuroAiD respectively collected clinical data at baseline and monthly visits (V) 1 to 3. Outcome measures included compliance, side effects, Glasgow Coma Scale (GCS), modified Rankin Scale (mRS), National Institutes of Health Stroke Scale (NIHSS), and Short Orientation-Memory-Concentration Test (SOMCT).

Results: Sixty-six subjects were included. NeuroAiD was well-tolerated with fair compliance over 3 months. Two non-serious side effects were reported. Mean scores significantly improved in all outcome scales. The proportion of subjects with favorable outcomes improved from baseline to V3: GCS 13-15, from 64% to 88% (p=0.007); mRS 0-1, from 9% to 37% (p=0.004); NIHSS 0-4, from 12% to 59% (p<0.0001); and SOMCT score 0-8, from 44% to 68% (p=0.029).

Conclusions: NeuroAiD in the real-world setting was safe and showed potential for a sustained positive result on neurological recovery after ICH.
ASSOCIATION BETWEEN AIR POLLUTION AND POST STROKE DEPRESSION & COGNITIVE DECLINE.

Sakshi Sharma¹, Mv Padma Srivastava², Neha Kuthiala¹
¹ALL INDIA INSTITUTE OF MEDICAL SCIENCE, Neurology, NEW DELHI, India, ²AIIMS, New Delhi, Neurology, Delhi, India

Background and Aims:: Stroke affects the cognitive domain, which includes attention, memory, language, and orientation. Air pollution is one of a variety of man-made environmental disasters that are currently taking place all over the world. To examine the associations of gaseous air pollutants and climate change (humidity& temperature) and depression including cognitive decline.

Methods:: All strokes: acute (within two weeks from onset) & chronic (within one year of event) presenting to the Neurology and Emergency services of AIIMS, were screened & recruited. Gaseous air pollutants and PM 2.5 & PM10 in diameter were measured in me Delhi designated areas using the help of Delhi Pollution Control Board at onset of stroke, 15 days of enrollment & 3 months. Stroke demographics and PHQ-9, GAD-7, SF-36 were correlated with the air pollution and climate change.

Results:: 90 patients were recruited. We found that depression and anxiety levels were high among the stroke patients. PM2.5 & PM10 levels were statistically related to stroke onset, depression & anxiety. The mean PM10 level was high as compared to PM-2.5 at all-time points indicating that higher particulate or coarse particles are better measured than the fine particles and its associated with cognitive decline & anxiety. We observed that the high level of particles effect on cognition and cause of depression. Multivariate regression analysis keeping age, type of stroke as constant with covariables like type of fuel, CO, PM2.5 showed R²= 0.119, F=3.92, p=0.057.

Conclusions:: We found that cognitive decline and depression is common in stroke patients but its also associated with high level of air pollution & climate changes. We need more results for final conclusion.
CORTICAL REORGANIZATION IN STROKE PATIENTS USING UPPER-LIMB ROBOTIC REHABILITATION THERAPY

Megha Saini¹, Neha Singh¹, Nand Kumar², S Kumaran³, Amit Mehndiratta¹, Mv Padma Srivastava⁴
¹Indian Institute of Technology, Centre For Biomedical Engineering, New Delhi, India, ²ALL INDIA INSTITUTE OF MEDICAL SCIENCES, Department Of Psychiatry, New Delhi, India, ³ALL INDIA INSTITUTE OF MEDICAL SCIENCES, Department Of Nmr, New Delhi, India, ⁴All India Institute of Medical Sciences New Delhi, Neurology, New Delhi, India

Background and Aims:: Coexistence of myriad of sensorimotor-impairments in stroke limit patient's functional-capacity. In current-scenario robotic-therapy involving objective strategies enhance motor-restoration. We aimed to analyze cortical-remapping after robotic-therapy in association with clinical-parameters.

Methods:: Low-cost, 3D-printed hand-exoskeleton has been designed in-house at IIT and AIIMS, New-Delhi, India. Six right-handed, left-hemiparetic patients with 3-24 months chronicity were recruited; with three patients(mean-age=37.33±5.03 yrs) in control-group and three patients(mean-age=38.33±16.44 yrs) in robotic-therapy group. All patients underwent 20-sessions of 45-minutes therapy each. Clinical-assessment(MAS, Fugl-Meyer Scale, Barthel-Index, mRS), cortical-excitability measure (RMT), neuroimaging (fMRI) were performed pre and post-intervention. Block-design paradigm of 40-seconds alternate baseline and activation-task were used. Patients performed self-paced wrist-extension repeatedly in full Range-of-Motion with affected-hand. fMRI-data were acquired as 31 slices, TR=2000ms, TE=30ms, FOV=230x230x155mm, Flip angle:90°, voxel-size:1.8x1.8x5 mm.

Results:: All six patients showed clinical-improvement using clinical-scales. Robotic-therapy was effective in reducing spasticity at wrist (1.66±0.28 to 1.33±0.57) compared to control-group (2±0 to 2±0), increase independence in ADL as demonstrated by Barthel-Index(75±13.2 to 93.33±5.77) compared to control-group(66.66±17.55 to 80±13.22). Sensorimotor-control improvement was established in both groups (37.33±6.6 to 46.66±6.5) in robotic-therapy compared to control-group (29.33±7.63 to 42±5.85). Resting Motor Threshold a measure of cortical-excitability demonstrated better improvement with robotic-therapy (87.66±2.51 to 71.33±8.08) versus control-group (87.33±12.50 to 84±16). Ipsilesional-activation pattern(BA4=12,BA1=33) and contralesional-activation(BA4=139,BA6=27,BA1=59 and BA5=13) was observed in robotic-therapy group(Fig1). Activation of contralesional-cerebellum(voxels=272) and ipsilesional-cerebellum(voxels=34) was observed in control-group(Fig1).

Conclusions:: Activation in ipsilesional-cortex indicates improved recovery reorganizational-pattern in stroke as compared to activation of contralesional-cortex or cerebellar-regions. Robotic-therapy is effective post-stroke rehabilitation-paradigm that can enhance recovery by means of use-dependent
plasticity.

**Fig 1:** BOLD activation pattern showing activation volume in functional MRI for affected hand movement at 10 voxel thresholds and FEW corrected at $p=0.05$ 
(a.) Robotic-therapy (b.) Control-group
MICRO-EMBOLIC SIGNAL (MES) MONITORING IN STROKE SUBTYPES: A SYSTEMATIC REVIEW AND META-ANALYSIS OF 58 STUDIES

Pachipala Sudheer, Shubham Misra, Manabesh Nath, Pradeep Kumar, Deepti Vibha, Mv Padma Srivastava, Manjari Tripathi, Rohit Bhatia, Awadh Pandit, Rajesh Singh
All India Institute of Medical Sciences, Neurology, Delhi, India

Background and Aims:: Micro embolic signals(MES) detected using transcranial doppler(TCD) help in risk stratification in stroke patients. A systematic review and meta-analysis was performed to estimate the prevalence of MES and its association with stroke recurrence, functional outcome and mortality in different stroke subtypes.

Methods:: A comprehensive literature search was conducted before 26th January 2021 in PubMed, Embase, Google scholar, Cochrane library and ClinicalTrials.gov. Studies were identified that used TCD to detect MES in stroke/TIA patients. Pooled prevalence and Odds Ratio (OR) along with 95% Confidence Interval (95%CI) were calculated for different outcome measures. Entire statistical analysis was conducted in R version 3.6.2.

Results:: 58 studies involving 5123 patients (1329 MES +, 3794 MES -) were included in our meta-analysis. The pooled prevalence of MES among all acute stroke/TIA patients was 30% (95%CI 25% to 34%). Prevalence of MES was high among all stroke subtypes except in patients with small vessel disease (SVD). In patients with new onset stroke/TIA, presence of MES was associated with high risk of recurrence of cerebral ischemia (OR 3.71; 95%CI 2.64 to 5.23). Although there was no significant association of presence of MES with increased mortality (OR 1.84; 95%CI 0.91 to 3.70) and poor functional outcome (OR 2.11; 95%CI 0.69 to 6.49) among patients with new onset stroke/TIA, this could only be determined in a smaller sample size of 477 patients.

Conclusions:: Presence of MES increased the chance of recurrence of cerebral ischemia but was not associated with poor functional outcome and mortality in the studied subgroup.
SAFETY AND EFFICACY OF N ACETYLCYSTEINE AS AN ADJUNCT TO STANDARD TREATMENT IN PATIENTS WITH ACUTE ISCHEMIC STROKE - A RANDOMIZED CONTROLLED TRIAL (NACTLYS)

Snigdha Komakula¹, Rohit Bhatia¹, Mv Padma Srivastava¹, Manjari Tripathi¹, Deepti Vibha¹, Mamta Singh¹, Ajay Garg², Leve Joseph², Rajesh Singh¹, Roopa Rajan¹, Anu Gupta¹, Awadh Pandit¹, Vishnu V Y¹

¹AIIMS, Neurology, NEW DELHI, India, ²AIIMS, Neuroradiology And Neurointervention, NEW DELHI, India

Background and Aims:: There is a clinical need for thrombolytic agents that can disaggregate arterial thrombi without significantly increasing the risk of bleeding. We aimed to study if adjunctive therapy of N-acetylcysteine (NAC) along with recombinant tissue plasminogen activator (rtPA) was safe and effective in patients with acute ischemic stroke.

Methods:: IV NAC with IV rtPA or IV rtPA alone was given in a 1:1 ratio in this open label randomized blinded assessor pilot study. Primary or safety outcomes were any intracerebral hemorrhage (ICH) or symptomatic cerebral hemorrhage (SICH), any systemic bleeding and any adverse reactions. Secondary or efficacy outcomes were major neurological improvement at 24 hours, recanalization on first run of angiography or on vascular imaging at 24 hours, mRS and mortality at 3 months of followup.

Results:: Out of 38 patients enrolled, 20 were in control arm and 18 in the intervention arm. Among primary outcomes, no significant difference was noted in the adverse reactions (p=0.99), ICH (p=0.21), SICH (p=0.47) and extracranial bleeding (p=0.21). Among the secondary outcomes, 7 patients (38.8%) in the intervention arm and 3 patients (15%) in the control arm had major neurological improvement at 24 hours (p=0.19). Proportion of patients with good outcome at 3 months (mRS 0-2) (p=0.84) and mortality at 3 months was similar in both the groups (p=0.65).

Conclusions:: NAC as an adjunct to rtPA did not show any significant difference in morbidity and mortality at three months. However, there was a favourable trend towards higher recanalization and early neurological improvement with co-administration of NAC and rtPA. Future larger trials are needed to further conclude on safety and efficacy of N-acetylcysteine as a thrombolytic agent.
**Background and Aims::** Basilar artery occlusion accounts for 11-39% of posterior circulation strokes, being prevalent in elderly population, with a wide-ranging clinical presentation. Consequently, its diagnosis may be particularly challenging and subtle symptoms might lead to misdiagnosis.

**Methods::** A 22 years-old woman referred for episodes of hyperventilation and stiffness at four limbs. She reported the same morning transient right ear tinnitus, paresthesia in right half face and hand. Her family mentioned a story of anxiety disorder with self-harm treated with sertraline, while cardiovascular risk factors, estroprogestinic or drug assumption were excluded. At neurological examination patient appeared mutacic, with dystonic posturing at four limbs, without signs of other functional systems involvement.

**Results::** Urgent brain CT scan was normal. She underwent psychiatric evaluation which ended up for acute anxiety crisis. In the following 48 hours patient reported decline in consciousness, with fever and desaturation. Another CT scan revealed no abnormalities, while electroencephalogramp profile excluded metabolic or irritative etiology. Cerebrospinal spinal fluid examination was unremarkable. Urgent MRI revealed a large subacute infarct involving the width of pons and part of mesencephalus and medulla oblungata, due to basilar artery occlusion extended for 18 mm, further confirmed by angioCT. Vascular studies showed no dissemination or fibromuscular dysplasia, hypercoagulation and cardiac investigation disclosed no significant contributing factor.

**Conclusions::** Although uncommon, this case represents a possible pitfall in clinical practice: neurologists should be aware that subtle clinical presentations, especially in young and low-risk patients, might hide severe conditions as basilar artery occlusion which require a prompt diagnosis in order to prevent following neurological disability.
CLINICAL UTILITY OF INTRAVASCULAR ULTRASOUND (IVUS) IN CAROTID ARTERY INTERVENTIONS - A SYSTEMATIC REVIEW AND META-ANALYSIS.

Biswamohan Mishra¹, Awadh Pandit², Shubham Misra³
¹AIIMS, New Delhi, Neurology, Delhi, India, ²All India Institute of Medical Sciences, Neurology, Delhi, India, ³AIIMS, New Delhi, Neurology, New Delhi, India

Background and Aims:: IVUS and its extension VH (Virtual Histology) IVUS evaluate plaque characteristics in real time and guide decision making during stenting. To date there is no consensus about indications of IVUS and its validated methods. This systematic review and meta-analysis aims to evaluate the clinical utility of IVUS in carotid artery stenting and develop a future consensus for research and practice parameters.

Methods:: A systematic review and meta-analysis was performed of articles published till February 2021. Studies reporting on IVUS parameters and findings and also its performance compared to other imaging modalities were included in study. Pooled prevalence with 95% Confidence Intervals (95%CI) were calculated. The statistical analysis was conducted in R version 3.6.2.

Results:: A total of 1825 patients from 30 studies were included. Meta-analysis performed on 1566 patients from 11 studies. In nine studies, stroke/TIA had a pooled prevalence of 4% (95%CI 3-5%) (Figure 1) while asymptomatic stroke had a pooled prevalence of 46% (95%CI 31-62%) in four studies (Figure 2). Two studies reported that IVUS detected more Plaque protrusion (PP) compared to angiography (n= 33/396 vs. 11/396), with PP group having higher stroke risk. IVUS led to stent type or size change in 8 of 48 cases in three other studies. Concordance between VH IVUS and true histology
was at 80-85% reported in 2 studies.
Conclusions: This study showed though IVUS fared better to CTA/MRA/angiography for better stent selection during CAS, however large scale, preferably randomized controlled studies are needed to predict its role in determining clinical outcome.
POSTERIOR CIRCULATION WAKE-UP STROKE AND CT PERFUSION: EFFECTIVENESS AND SAFETY OF REPERFUSION THERAPY

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Background and Aims:: Patients waking up with acute ischemic stroke (AIS) represent an underprivileged subgroup of stroke patients. Because in wake-up stroke (WUS) time of symptom onset is unknown, best management is challenging. Patients with WUS involving posterior circulation stroke represent an even more delicate subgroup. Use of multimodal computed tomography (mCT), combination of non-contrast CT, CT angiography and CT perfusion (CTP) is generally used in anterior ischemic strokes to identify candidates for reperfusion therapies; its use in posterior AIS has not been widely accepted. We aimed to describe effectiveness and safety of CTP in evaluation of posterior-WUS patients eligible for reperfusion treatment.

Methods:: We included patients with posterior-WUS who underwent thrombolysis treatment at Trieste Stroke Unit between March 2016 and October 2019. All patients underwent mCT and neurological evaluation. Out of 80 patients with WUS, there were 21 posterior-WUS.

Results:: In all those patients CTP showed abnormalities. All 21 patients underwent thrombolysis, 3 also underwent thrombectomy. Large vessel occlusion was reported in 14 cases (3 basilar artery, 7 vertebral artery, 4 posterior cerebral artery occlusion). Outcome given by NIHSS score at 7 days and mRS score at discharge (1 and 3 months) was favorable in all cases (NIHSS at 7 days: 1(0-42); mRS at 1 months ≤2: 16/21; mRS at 3 months <2: 11/21). Reperfusion therapy was safe in all cases (sICH: 0/21).

Conclusions:: CTP-guided reperfusion therapy was associated with improving outcome and safety profile.
Background and Aims:: Early neurological deterioration (END) in acute ischemic stroke occurs frequently. This phenomenon has a heterogeneous pathomechanism. Immature platelet fraction (IPF) is known as the useful marker of increased platelet production and turnover which could occur in patients with increased platelet activation. We investigated whether the IPF is associated with the prevalence of END in acute ischemic stroke patients.

Methods:: A total 1655 of acute ischemic stroke patients in single tertiary academic center was enrolled from January 2013 to October 2018 via stroke registry. IPF levels were quantified by whole blood flow cytometry with automated assays (Sysmex XE-2100™). High IPF was defined as the IPF level was more than 5%. Early neurological deterioration was defined as an increment change of at least one point in motor power or total National Institute of Health Stroke Scale (NIHSS) score deterioration ≥2 points within the first week after admission.

Results:: A total of 72 patients (4.4%) experienced END. END was more prevalent in the patients with high IPF [13 (11.7%) vs 59 (3.8%), p<0.0001]. Multivariate logistic regression analysis showed high IPF was an independent predictor of the prevalence of END (adjust odds ratio = 1.32; 95% confidence interval = 1.03–1.70).

Conclusions:: A high IPF levels was associated with the prevalence of END in acute ischemic stroke patients.
ESTIMATION OF THE BURDEN OF ATHEROSCLEROSIS IN STROKE DUE TO CRANIOCERVICAL DISSECTION- A CLINICORADIOLOGICAL STUDY

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Background and Aims:: The etiology of craniovertebral dissection is not fully understood. Atherosclerosis being a pro-inflammatory state might be a predisposing factor. Indians, as well as South Asians, are unique in that, they have a high burden of atherosclerosis. This study was planned to find a consortium between dissection and atherosclerosis by radiological imaging and estimation of vasomotor reactivity by TCD

Methods:: This study was carried out at a tertiary care institute in North India and included dissection (31), stroke (31) and 29 controls. All subjected for a TCD study, vessel wall and neuroimaging for parenchymal evidence of atherosclerosis and infarct pattern

Results::

Prevalence of atherosclerosis and stenosis (>50% ) was higher in Group(B) compared to (Group A) (p=0.05) and (p=0.007) respectively. In (Group A), patients with long-segment atherosclerosis, and higher thickness of plaque are significantly more likely to have infarcts > 5mm in size and long segment arterial dissection (p=0.005)
Conclusions:: Our results suggest that atherosclerosis to play at least some role in the causation of CAD as well as in its consequences such as size of infarcts.
EARLY CHILDHOOD GROWTH AND RISK OF ADULT CEREBROVASCULAR DISEASE DASH THE NORTHERN FINLAND BIRTH COHORT STUDY 1966

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Background and Aims:: Low birth weight is associated with increased risk of adulthood cerebrovascular disease. Not much is known about effects of early childhood growth. We studied whether the risk of cerebrovascular disease in adulthood is associated with growth or nutritional factors during early childhood.

Methods:: Within the Northern Finland Birth Cohort 1966, 11,991 persons were followed from birth to 52 years of age. Cerebrovascular disease diagnoses came from national hospital and death registers with diagnostic coding based on the World Health Organization classification. Cox proportional hazard models were used to estimate associations of childhood growth variables, growth trajectories (by Latent Class Growth Modelling) and nutritional factors with adult cerebrovascular disease. The analyzes were adjusted for socioeconomic status and birth weight.

Results:: 453 (3.8%) cerebrovascular diseases were recorded. Among women, the trajectory groups of consistently low weight and length had an increased risk for ischemic strokes, with an adjusted hazard ratio (aHR) of 1.97 (95% confidence interval (CI) 1.21-3.20) and 2.05 (95% CI 1.11-3.81), respectively. In addition, women with BMI over 1 SD at BMI rebound had an increased risk for ischemic stroke (aHR 1.90; 95% CI 1.19-3.04) compared to women with BMI -1 to +1 SD. These associations were not found among men.

Conclusions:: Women who are short and light in early childhood or who have high BMI at BMI rebound have as adults increased rates of ischemic strokes. These findings suggest that timing of weight gain during childhood is of significance for development of cerebrovascular disease risk.
SERUM S100B PROTEIN AND GLASGOW COMA SCALE AS PREDICTIVE MARKERS OF THE SURVIVAL RATE IN ACUTE ISCHEMIC STROKE

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Background and Aims:: Serum S100β is increasing after acute ischemic stroke (AIS), and peaking within 72 hours and correlating with the volume of damage and clinical symptoms. Our postulate is that evaluation of serum S100β after 48-72 hours from onset of AIS and assessment of the patient's level of consciousness on the Glasgow Coma Scale (GCS) is suitable to predict of survival rate and/or life-threatening outcome of early rehabilitation in the first 14 days of AIS.

Methods:: Serum S100β was determined by using DY1820-05 Human S100β DuoSet ELISA-kit (USA) of 105 patients after 48-72 hours from onset of AIS in the middle cerebral artery (middle age=63(57;67) years, NIHSS=16(8;23) points, GCS=13(11;15) points). The predictive model was constructed by logistic regression method. The critical values for categorical variables were identified by ROC-analyses.

Results:: The cut-off points: S100-β=13.3 (sensitivity 95.5%; specificity 72.0%; sum 167.5%); GCS=14 (sensitivity 87.4%; specificity 84.0%; sum 171.4%). The characteristics of logistics regression model: Chi-square=64.7; p<0.001, Nigel-Kirk's coefficient=0.72; 94.9% sensitivity and 72% specificity; percentage of correct decisions 89.3%. Serum S100-β ≥13.3 pg/ml decrease the chances of survival by a factor of 58.1 and prognostically favorable (95% CI[10.0-339.6], p<0.001). The GCS≥14 points increases the chances of survival by a factor of 24.5 and prognostically favorable (95% CI[4.6-130.3], p<0.001).

Conclusions:: Quantitative features of S100β and GCS after 48-72 hours from onset of AIS are allowed stratifying patients into a group with a high risk of lethal outcomes. This predictive model is convenient to use for rapid assessment of survival and solving issues of doses of mobilization on safety outcomes of early rehabilitation.
COMPARISON OF THE NEW CANADIAN SCORE TO ABCD2 FOR TIA RISK STRATIFICATION IN A COMMON CLINICAL SETTING

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Background and Aims: INTRODUCTION Patients who have a TIA are at high risk of subsequent stroke, especially in the short term. The degree of risk is usually determined using clinical scores, most commonly ABCD2. Recently, a new score (Canadian TIA Score) has been proposed, which may be better in terms of prediction, and which includes more variables, both clinical and instrumental (i.e. presence of AF, carotid stenosis, any infarction on CT). We aimed at evaluating whether the two scores were reproducible, using data from our admission registry.

Methods: MATERIAL AND METHODS We retrospectively analysed prospectively collected data from our Stroke Unit registry in 2018 and 2019. We recalculated ABCD2 and de novo calculated CTS for each patient. Then we compared the two scores both with Spearman rank correlation and with Cohen Kappa, using commonly defined cutoff points (4 for both scores, which would have been used to decide whether to admit the patients or not).

Results: RESULTS There were 51 patients. Median ABCD2 was 4 and median CTS was 9. Spearman rank correlation was 0.64 (p<0.001), whereas Kappa statistics gave a value of 0.35 (fair agreement).

Conclusions: CONCLUSION The two scores are only moderately reproducible. However, since the decision to admit the patient is usually based both on scores and on other information (which are included in the Canadian score, but not in ABCD2), it would be useful in the future to compare the common clinical practice (including ABCD2 score use) to the Canadian score, which, however, seems less practical to use in an emergency settings.
CEREBRAL VENOUS THROMBOSIS IN SUB-SAHARAN AFRICA: A SYSTEMATIC REVIEW

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Background and Aims: The global clinical epidemiology of cerebral venous thrombosis (CVT) is well described in high-income countries and in some middle-income countries, where hospital-based case series, suggest that the frequency of CVT is probably higher than in high-income countries.

Methods: We followed Meta-Analysis of Observational Studies and observational studies reporting original data on any of demographics, etiology, clinical and neuroimaging features, associated conditions, treatment, functional outcome and mortality in Sub-Saharan Africa.

Results: Notificação de 274 pacientes com TVC Em ambos os relatos de casos e séries de casos, a cefaleia foi o sintoma de apresentação mais comum (92,3% e 71,6% em relatos de casos e séries de casos, respectivamente), seguido por déficits neurológicos focais (38,5% e 23,8%).
Table 1. Summary of 274 patients with cerebral vein thrombosis from Sub-Saharan countries

| Age            | Minimum-maximum | Number | %    | Valid %
|----------------|-----------------|--------|------|--------
| Females        | 8 months-78 years | 153    | 55.8 | 58.6   |

Associated conditions

| Condition                    | Number | %    | Valid %
|------------------------------|--------|------|--------
| Infection                    | 173    | 63.1 |        |
| Contraceptives               | 29     | 7.3  |        |
| Pregnancy & puerperium       | 17     | 6.2  |        |
| Thrombophilia                | 6      | 2.2  |        |
| Antiphospholipid syndrome    | 4      | 1.5  |        |
| Protein S deficiency         | 2      | 0.7  |        |
| Cancer                       | 4      | 1.5  |        |
| Behçet's disease             | 6      | 2.2  |        |
| Other systemic disease       | 4      | 1.5  |        |
| Trauma                       | 1      | 0.4  |        |
| Epidural anaesthesia         | 1      | 0.4  |        |

Symptoms and signs

| Symptom                      | Number | %    | Valid %
|------------------------------|--------|------|--------
| Count not stated             | 13     | 4.76 |        |
| Headache                     | 187    | 68.2 | 71.6   |
| Neck pain/stiffness          | 36     | 13.1 | 13.8   |
| Papilloedema                 | 22     | 8.0  | 8.4    |
| Visual disturbances          | 11     | 4.0  | 4.2    |
| Focal deficits               | 62     | 22.6 | 23.8   |
| Seizures                     | 44     | 16.0 | 16.9   |
| Decreased alertness          | 13     | 4.7  | 4.9    |
| Cavernous sinus syndrome     | 38     | 13.8 | 14.6   |
| Other cranial nerve palsies  | 21     | 7.7  | 8.0    |

Neuroimaging diagnostic methods

| Method                        | Number | %    | Valid %
|-------------------------------|--------|------|--------
| No information                | 40     | 14.6 |        |
| CT                            | 199    | 72.6 | 85.0   |
| MR/IVP venography             | 57     | 20.8 | 24.4   |

Thrombosed sinus/veins

| Vein                          | Number | %    | Valid %
|-------------------------------|--------|------|--------
| No information/no counts      | 30     | 10.9 |        |
| Superior sagittal             | 61     | 22.2 | 25.0   |
| Transverse/sigmoid            | 143    | 52.2 | 58.6   |
| Straight                      | 9      | 3.3  | 3.7    |
| Deep venous system            | 7      | 2.6  | 2.9    |
| Cavernous                     | 38     | 13.9 | 15.6   |
| Cortical vein                 | 12     | 4.4  | 4.9    |

Anticoagulation

| Anticoagulant                 | Number | %    | Valid %
|-------------------------------|--------|------|--------
| No information                | 51     | 18.6 |        |
| UF heparin                    | 121    | 44.2 | 54.3   |
| LMWH                          | 35     | 12.8 | 15.7   |
| VKA                           | 86     | 31.4 | 38.6   |

Deaths

| Death                         | Number | %    | Valid %
|-------------------------------|--------|------|--------
| No information                | 64     | 23.4 |        |
| Death                         | 21     | 7.7  | 10.0   |

Sequels

| Sequel                        | Number | %    | Valid %
|-------------------------------|--------|------|--------
| No information                | 145    | 52.9 |        |
| Complete recovery             | 60     | 21.9 | 46.5   |
| Partial recovery              | 48     | 17.5 | 37.2   |

*Only shown if there was missing data.
UF = unfractionated LMWH = low molecular weight heparin VKA = vitamin K antagonist.
Conclusions: The low number of reported CVT cases from Sub-Saharan Africa suggests that CVT is either infrequent, not diagnosed or not reported. Infection is the most common risk factor. Most CVT cases were confirmed by CT alone. Almost all patients reported after year 2000 received anticoagulation. Death rate was higher than in high income countries.
Background and Aims:: Diffusion-weighted magnetic resonance imaging (DW-MRI) is considered to be a sensitive tool to detect an acute stroke. However, MRI may not be 100% sensitive in very early stages, especially in posterior circulation strokes.

Methods:: We present the case of a 67-year-old diabetic, hypertensive female who presented with unresponsiveness with right-sided reduced movements and facial deviation of 30 minutes duration. (BP 130/72, RBS 129, INR 1.2). Non-contrast computerized tomography (NCCT) of the brain was unremarkable. (ASPECTS 10), CT angiogram did not show any large vessel occlusion (Figure 1 a and b) and MRI brain (2.5 hours of symptoms) was negative (Figure 2 a).

Figure 1 a Non-Contrast CT showing no infarct. b CT angiogram showing no large vessel occlusion
Results:: Although initial DW-MRI was negative, the repeat MRI brain on day 5 revealed infarcts in the left midbrain and bilateral thalami. (Figure 2b). The patient was thrombolysed (Window Period: 45 minutes) with IV alteplase (door to CT time of 5 minutes and door to needle time of 20 minutes). 24 hours post thrombolysis, NIHSS improved to 6, and alertness improved when she also noticed double vision. Examination showed a left 3rd nerve palsy with pupillary involvement. Diplopia and weakness gradually improved over 2 days (NIHSS 2).

Conclusions:: Artery of Percheron stroke with unremarkable initial MRI-DWI, a repeat MRI after 24 hours of consistent neurological deficit is more demonstrative. Our case serves as a reminder that clinical assessment shall be the priority until a diagnostic modality showing 100% sensitivity and specificity are evident and our report also emphasizes that negative DW-MRI with clinical presentation of stroke should not preclude thrombolysis.
COMPARISON OF CODE STROKE RESPONSE TIMES BETWEEN THE EMERGENCY DEPARTMENT AND INPATIENT SETTING IN A MAJOR METROPOLITAN HOSPITAL

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Background and Aims:: In stroke care, speed is essential for good outcomes. Opportunities for speed improvements have been extensively documented in the medical literature. This retrospective study is aimed at providing data and insights for the development of a quality improvement project in the same hospital, with the ultimate goal of increasing code stroke speed response times without compromising quality of care.

Methods:: All code stroke cases with a CT scan were included. Data were collected between January and December 2020, from both emergency department and inpatient settings. Emergency room stroke code times were compared with those in the inpatient setting by using a two-tailed t-test and a 95% confidence interval.

Results:: Statistically significant p values were observed for a difference between ED and inpatient code-to-CT start times for both thrombolysed and non thrombolysed events. Code-to-CT read times for events that did not go into t-PA administration also had a p value smaller than 0.05.

Conclusions:: This study highlights the urgent need to improve code-to-CT times in this hospital’s inpatient setting, since ED code stroke times were markedly better from a statistical viewpoint. Improving quality of care will have to address the evident delay in transporting inpatients to the CT scan after a code stroke has been activated. This study calls for the enactment of a CT-first comprehensive new protocol, aimed at helping to mitigate inpatient delays and further enhance the quality of the care provided. The approach discussed may be valuable to the improvement of other services in the region.
Background and Aims:: A clinical audit was undertaken to measure time intervals including door-to-needle time (DNT) and factors affecting major steps of stroke thrombolysis and to develop a protocol to optimize acute stroke care at National Hospital Kandy (NHK).

Methods:: A standards-based clinical audit was conducted among acute ischaemic stroke (AIS) patients presenting to NHK. Data on emergency care, time intervals, pre-hospital data and awareness of stroke and available facilities were collected using an interviewer administered data collection sheet.

Results:: The median DNT in 28 patients thrombolyzed over a period of 7 months was 70 minutes. Being male was associated with a statistically significant likelihood of receiving thrombolysis. Out of the 5 pre-specified audit criteria, initial evaluation and interpreting the CT brain met the targets. Door-to-CT time, informing neurology team and DNT failed to meet the pre-specified targets. In 28 non-thrombolyzed AIS patients, late presentation and intra-hospital delays were the commonest causes for conservative management. Waiting for the official CT brain report to inform neurology was the commonest intra-hospital delay. Only 26.8% were aware of stroke thrombolysis, 80% of whom knew about a time limit. 66.6% knew it was available at NHK. 85.7% were aware of the island-wide free ambulance service, however only 58.3% knew the toll-free telephone number and only 12.5% AIS patients used the service.

Conclusions:: Several factors have contributed to unsatisfactory DNTs at NHK. A 'stroke code' and an 'acute stroke pathway' was introduced to optimize AIS care and re-analysis is currently being conducted to assess outcome.
RELATIONSHIP BETWEEN SLEEP DISTURBANCES AND QUALITY OF LIFE IN THE PATIENTS AFTER ISCHEMIC STROKE.

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Background and Aims:: To evaluate the interaction between the subjective sleep quality and the quality of life in patients who had an ischemic stroke.

Methods:: We examined 80 patients (men - 44, (55%) women - 36, (45%), aged from 40 to 78 years, average age – 60.37 ± 0.95 years) in post-stroke patients with ischemic type at the Tashkent Medical Academy in neurology department. The Pittsburgh questionnaire was used for determining the quality of sleep index (PSQI). The quality of life (QOL) was assessed with “SF-36 Health Status Survey” taking into considerations two parameters - mental health and physical health.

Results:: On the Pittsburgh scale, various sleep disorders were observed in 70 patients (88%) 100% of cases from 1 to 5 times a week) in relation to the duration of sleep, daytime dysfunction, and subjective sleep quality. Poor sleep quality (higher PSQI components (19–29 points) were observed in patients with ischemic stroke, the average PSQI score was 0-5 points). According to “SF-36 Health Status Survey”, it was established that, in post-stroke patients who had suffered from ischemic stroke, demonstrated decreased parameters in physical sphere of the QOL, whereas mental health was within the control parameters. Concerning sleep quality, the greater sleep scores were the worse QOL would be.

Conclusions:: In addition to physical and mental impairment resulting from stroke itself, the presence of sleep disorders impact negatively QOL in ischemic stroke patients. Therefore, diagnosing and treating sleep disorders is of a great importance in ischemic stroke patients to optimize their functional outcome and improve their QOL.
IMPROVING ACUTE STROKE ASSESSMENT IN NON-ENHANCED CT: AUTOMATED TOOL FOR EARLY ISCHEMIC LESION VOLUME DETECTION

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Background and Aims:: The ASPECTs is a widely adopted marker to identify early stroke signs on non-enhanced CT (NECT), but it presents inter-individual variability and it can be hard to use for non-experts. We introduce an algorithm capable of estimating automatically the NECT volumetric extension of early acute ischemic changes in the 3D-space. We compared the power of this marker with ASPECTs evaluated by experienced practitioner in predicting the clinical outcome.

Methods:: We analyzed and processed neuroimaging data of 153 patients admitted with acute ischemic stroke. All patients underwent a NECT at admission and on follow-up. The developed algorithm identifies the early ischemic hypodense region appearing based on an automatic comparison of the gray level of the images of the two hemispheres.

Results:: The volume marker and the ASPECTs agree in 66% of the patients. In the two standard axial slices used to estimate the ASPECTs, the regions identified by the algorithm overlap significantly with those identified by experienced practitioners. However, in many patients the regions identified automatically extend significantly to other slices. In these cases, the volume marker provides supplementary and independent information. Indeed, the clinical outcome of patients with volume marker=0 can be distinguished with higher statistical confidence than the outcome of patients with ASPECTs=10.

Conclusions:: The volumetric extension and the location of acute ischemic region in the 3D-space, identified automatically by our algorithm, provide an information which is mainly consistent with the ASPECTs value decided by expert practitioners, but is often complementary and independent.
Background and Aims:: There is a lot of experimental and clinical evidence that atherosclerosis is a chronic inflammatory disease with an autoimmune component. Endothelial damage causes a cascade of inflammatory reactions involving monocytes, macrophages, T-lymphocytes, and vascular smooth muscle cells. The aim - to study the ability of vascular wall’s smooth muscle cells to change their phenotype and their involvement in immune responses in cerebrovascular atherosclerosis.

Methods:: The total of 50 individuals deceased of cerebral atherosclerosis, 50 - without ischemic stroke and 20 deceased from causes not associated with atherosclerosis (comparison group) were studied. The following markers were used: CD4, CD8, CD20, CD68, Actin Smooth Muscle Ab-1, Desmin, Vimentin.

Results:: Under ischemic strokes and severe atherosclerosis the cerebral vessels endothelium acquires structural changes in form of rupture, desquamation and exfoliation, formation of desquamated endothelial cells clusters. Speaking of endothelial damage, it should not be supposed that changes should occur at the macroscopic level only, endothelial damage at the cellular level shall be sufficient enough. Immunocompetent cells are of key importance in atherosclerosis development; adhesion on the luminal surface of arteries, presence of a large number of these cells under the endothelium and of more mature macrophages in the intima depth indicates the influx of these cells, which actively potentiate atherosclerosis formation, from the blood into the artery wall.

Conclusions:: Disorders of the endothelial lining with changes in endothelial cells morphology contribute to the atherosclerotic plaque development. Lymphocytes and macrophages form the molecular basis of many important processes, including the inflammatory response and the immune response.
THE ASSOCIATION BETWEEN HEMOGRAM PARAMETERS AND POST STROKE DEPRESSION

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Background and Aims:: Post-stroke depression (PSD) is the most common psychological consequence among stroke patients. Currently, patients with PSD has been reported with decreased quality of life, poor functional outcomes and increased mortality. Early recognition and diagnosis of PSD with accurate identification of novel risk factors is essential for clinicians to optimize patient care and management. Our aim was to assess the association between serum platelet to lymphocyte ratio (PLR) and serum neutrophil-to-lymphocyte ratio (NLR) at the admission day and the development of PSD at 3-month post-stroke.

Methods:: This cross-sectional study conducted in the Department of Neurology at the university hospital of Sahloul-Sousse-Tunisia. We included patients suffering from acute stroke between July 2018 and June 2019. Clinical characteristics, PLR and NLR at hospital admission were noted. PSD at 3 months were assessed with The Beck Depression Inventory (BDI).

Results:: A total of 250 stroke patients were included with mean age SD of 64±12.2 years 50.2 % men. Sixty percent of patients suffered from PSD. In the univariate analysis being male (p=0.004), admission National Institutes of Health Stroke Scale (NIHSS)(p<0.001) , presence of cognitive impairment assessed by Montreal Cognitive Assessment(p=0.021) , marital status (p=0.04), and poor functional outcome assessed by Modified Rankin Scale(p=0.001) were associated with PSD. Patients diagnosed with PSD had higher levels of PLR and NLR without significant association 112.93 vs 131.28 (p=0.148) and 2.48 vs 2.88 (p=0.132).

Conclusions:: Our findings suggest that Increased NLRs and PLRs at admission are found in patients suffering with PSD without significant correlation. It need to be validated by a larger trial.
STROKE-RELATED MORTALITY, DISABILITY AND ASSOCIATED FACTORS IN TWO REGIONAL HOSPITALS IN CAMEROON: A PROSPECTIVE COHORT STUDY

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Background and Aims:: Stroke is the second leading cause of death worldwide, causing 5.7 million deaths annually. Stroke mortality is seven times higher in low-income than high-income countries. Given the scarcity of data on stroke-related mortality and disability in Cameroon, this study aimed to estimate stroke mortality and disability in 2 Cameroonian hospitals.

Methods:: This was a prospective cohort study from January to July 2020, enrolling neurologist-confirmed stroke patients. Demographic and clinical data of stroke patients were collected using the WHO STEP questionnaire for hospital stroke surveillance. Survival and disability were assessed on the 7th (early mortality) and 30th days (overall mortality) post-stroke. Disability was assessed using the Modified Rankin Scale (mRS) and the Barthel index (BI). Deaths were confirmed from death reports by physicians in patient files and by verbal autopsy for discharged patients. Logistic regression was used to determine factors associated with mortality and disability.

Results:: Stroke mortality at 7 and 30 days were respectively 14.3% and 26.2%. On multivariate analysis, 30-day mortality was associated with altered consciousness (OR=5.462, P=0.008), haemorrhagic stroke (OR=2.980, P=0.027), and aspiration pneumonia (OR=11.677, P=0.004). One month (30 days) after stroke event, there were 62 survivors of whom 38.9%, 17.7%, 16.2%, and 40.3% were completely independent, partially independent, partially dependent, and totally dependent respectively. On multivariate analysis, poor functional outcome (dependence) was associated with severe stroke, NIHSS ≥16 (OR=8.321, P=0.011).

Conclusions:: Mortality and disability of stroke are high in our study population. Haemorrhagic stroke, severe stroke and presence of complications (dysphagia) were associated with worse outcomes.
ACUTE DIZZINESS AND VERTIGO IN CORTICAL STROKE: BIAS OF SUBJECTIVE RECALL

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Background and Aims:: Vertigo/dizziness may be early presenting symptoms of posterior circulation stroke. However, single case reports of isolated hemispheric strokes presenting with vertigo are present in the literature. We explored the prevalence of vertigo/dizziness in acute stroke and evaluated the cortical distribution of these lesions in relation to the known vestibular cortical network.

Methods:: We conducted structured interviews in 173 patients admitted to the hyperacute stroke unit in University College London Hospitals. The interview was used to evaluate whether the patient was suffering from dizziness and/or vertigo 1) before the onset of the stroke, 2) at the time of the stroke and 3) since the onset of the stroke.

Results:: In total 173 completed questionnaires were collected. A total of 71 patients had cortical infarcts with appropriate imaging registration for further analysis. Of these, 50 patients did not report any dizziness symptoms, 21 patients reported acute dizziness. Out of the total 71 patients with cortical infarcts, 31 patients had lesions in the vestibular cortical areas distributed within the insular and parietal opercular cortices, but only eight patients had acute dizziness.

Conclusions:: We found a low prevalence of vertigo in acute cortical strokes, with no single locus of lesion overlap. There is growing evidence supporting a lateralised vestibular cortex, with speculation that cortical strokes affecting the right hemisphere, are more likely to cause vestibular symptoms than left-hemispheric strokes. We observed a trend for this association, with the right hemisphere affected in 4 of 5 patients who reported spinning vertigo at the onset of the stroke.
WATERSHED INFARCTION ASSOCIATED WITH CEREBRAL VENOUS THROMBOSIS: BORDER ZONE CONGESTIVE CEREBRAL ISCHEMIA

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Background and Aims:: Cerebral venous thrombosis is a rare form of stroke (< 1%). It generally occurs in younger patients (< 50 years old) with high variability of clinical manifestations ranging from acute or chronic headache to coma. Its diagnosis is often delayed or overlooked, and imaging studies are essential for its identification being magnetic resonance with venography sensitive and specific technique to detect it. We report an unusual case.

Methods:: The methodology is a case report

Results:: 37-years-old male with headache and right focal neurological deficit of subacute evolution initially diagnosed as an acute ischemic stroke without clear etiology after routine evaluation. Due to the worsening of the headache originated 4 months ago with the initial event is retrospectively diagnosed with thrombosis of superior sagittal sinus when reviewing the old resonace (figure 1). It was also noted superficial and deep unilateral ischemic involvement in border zone on new resonance (figure 2). Low level of vitamin b12 was evidenced. The patient improved after starting cyanocobalamin, due to recanalization of the sagittal sinus it was not considered anticoagulation (figure 3). Figure 1.
Conclusions: There are few published data on the patterns of parenchymal damage in the context of venous stroke, and although there is no typical pattern or location, the lesion usually corresponds to the venous drainage territory. This is an unusual case because the pattern found was a unilateral border zone.
WHAT BECOMES OF PEOPLE WITH STROKE IN SUB-SAHARAN AFRICA 2-3 YEARS AFTER THEIR FIRST STROKE?

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Background and Aims:: Stroke is one of the leading causes of acquired disabilities in adults, accounting for increased morbidity and physical dependence. Very little is known about the outcome of stroke in sub-Saharan Africa. We therefore sought to determine the morbidity and mortality of stroke patients.

Methods:: We carried out a multi-center, hospital-based, cross-sectional study enrolling consenting stroke survivors, 2 years after their first stroke episode. Socio demographic and clinical data were collected using pre-established and standard questionnaires; Barthel index, Mini mental scale Examination, Hamilton depression scale, Short form-36 health survey. Information on deceased subjects were either obtained from hospital files or reported by their caregivers.

Results:: We enrolled 102 participants with a mean age was 65.04 ± 13.99 years (range: 22-96 years) out of who 70 (68.63%) died within 2-3 years after a first stroke. Out of 32 survivors, 28 (87.5%) had complications ranging from depression (71.9 %), musculo-skeletal pain (53.1 %), dementia (46.9 %), paresis/paralysis (40.6 %), recurrent stroke (31.3 %), seizures (28.1 %) varus deformity (30.3 %) and joint contracture (24.2 %). Among the survivors, 7 (25 %) were severely dependent and 6 (18.8 %) were moderately dependent. The majority of post-stroke subjects (62.5 %) were unable to work 2-3 years after a first stroke as a result of post-stroke disability (42.9 %) and incomplete recovery (33.3 %).

Conclusions:: Stroke is associated with significant disability, morbidity and mortality in Cameroon. Early diagnosis and a multi-disciplinary approach in the management could curb this trend.
CHARACTERISTICS OF STROKE IN TWO REGIONAL HOSPITALS IN CAMEROON

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Background and Aims:: The burden of stroke and its risk factors is increasing in low- and middle-income countries. Data have on the characteristics and risk factors of stroke in Africa are limited to tertiary hospitals. The aim of this study was to describe the characteristics of stroke in two Regional hospitals in Cameroon.

Methods:: This was a cross-sectional descriptive study among stroke survivors in the Bamenda and Buea Regional Hospitals over 5 months. Socio-demographic, clinical, and paraclinical data were recorded using a modified version of the WHO STEPwise questionnaire for stroke surveillance in hospitals.

Results:: A total of 84 participants were enrolled with a male/female sex ratio of 0.8. The mean age of participants was 64.8 ± 16 years. Ischaemic and haemorrhagic stroke represented 58.3% and 16.7% respectively. About one-quarter of all strokes were unclassified (absence of Brain CT). The main risk factors for stroke were hypertension (84.5%), diabetes mellitus (31%) and dyslipidaemia (31%). The median time from symptoms onset to consultation was 72 hours. The main clinical features on admission were hemiplegia (89.3%) and aphasia (56.0%). The most frequent complications were pressure sores (23.8%), and aspiration pneumonia (17.9%).

Conclusions:: Ischaemic strokes were the most common stroke types; hypertension was the most common risk factor while pressure sores and aspiration pneumonia were frequent complications of stroke in our sample. Urgent public health measures are needed in this population.
ONE AND A HALF SYNDROME AND BILATERAL CEREBELLAR ATAXIA AS A UNCOMMON BRAINSTEM STROKE.

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Background and Aims:: One-and-a-half syndrome, a term originally coined by Fisher in 1976 to describe a syndrome with horizontal movement disorder of eyeballs, presents a combination of ipsilateral conjugate horizontal gaze palsy (one) and ipsilateral internuclear ophthalmoplegia (INO) (a half). The diagnoses of one-and-a-half syndrome and its spectrum disorders rely on distinctive clinical symptoms, neuroanatomy, especially imaging technologies. On the other hand, ophthalmoplegia and bilateral cerebellar ataxia are not typical presentations that perplex the clinicians trying to look for a treatable cause such as multiple sclerosis, miller fisher syndrome, and brainstem encephalitis. However, a rare cause like brainstem stroke might be not considered.

Methods:: Case Report and literature review.

Results:: A 61-year-old diabetic and hypertensive lady presented with a history of acute onset dysarthria, dysphagia, double vision, and clumsiness in using her hands. Examination revealed ophthalmoplegia, one and a half syndrome, left facial weakness, and bilateral cerebellar signs. Brain MRI showed multiple bilateral small infarcts at the level of the midbrain and pons. Stroke work up included echocardiography and 24-hour Holter monitor both of which were normal studies. The patient was started clopidogrel and was referred for rehabilitation.

Conclusions:: One and half syndrome and Bilateral ataxia can be signs of multiple ischemic brainstem stroke. Clinicians should consider ischemic brain stroke first when they encounter a patient with such presentation to avoid unnecessary investigations and missing a treatable cause.
CONTRALATERAL DEEP MEDULLARY VEINS IS ASSOCIATED WITH POOR FUNCTIONAL OUTCOMES IN ISCHEMIC STROKE PATIENTS WITH ATRIAL FIBRILLATION AND/OR RHEUMATIC HEART DISEASE

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Background and Aims:: Little is known about the association between deep medullary veins (DMVs) and outcomes of ischemic stroke patients with atrial fibrillation (AF) and/or rheumatic heart disease (RD). Our aim is to investigate the prognostic implications of DMVs in ischemic stroke patients with AF and/or RD.

Methods:: Ischemic stroke patients with AF and/or RD (time from onset to admission ≤ 7 days) admitted to West China Hospital of Sichuan University were consecutively and prospectively enrolled between October 2013 and June 2018. Demographic, clinical and neuroimaging characteristics were collected. A four-grade scales (0: not visible, 1: < 5 conspicuous DMVs, 2: 5-10, 3: > 10; mild: 0-2, severe: 3) were used to assess the severity of DMVs on the contralateral hemisphere based on susceptibility-weighted imaging. Functional outcomes was classified as poor if the modified Rankin Scale (mRs) score was ≥ 3 at 3-month.

Results:: Of 170 patients, 149 presented with mid DMVs grades and 21 with severe DMVs. Those patients who presented with mild and severe DMVs differed significantly in NIHSS score, SBP, infarct lesion > 1/2 MCA territory, mRs scores and poor outcomes at 3-month (all p < 0.05) but not in age, gender, AF and/or RD, heart failure, stroke risk factors, treatments (prior or in hospital) and hemorrhagic transformation (p > 0.05). After adjustment for confounders, patients with severe DMVs were more likely to have higher mRs scores (OR 3.337; 95% CI, 1.351-8.248; p = 0.009) and poor outcome at 3-month (OR 5.830; 95% CI, 1.266-26.856; p = 0.024).

Conclusions:: A severe contralateral DMVs grade was independently associated with poor outcomes, indicating that it needs to be taken into account when assessing the prognosis. Further studies with larger samples are required to validate these findings.
A CASE OF ACUTE ISCHEMIC STROKE DUE TO INNOMINATE ARTERY THROMBOSIS TREATED BY EMERGENCY BRACHIOCEPHALIC ENDARTERECTOMY PERFORMED IMMEDIATELY AFTER IV THROMBOLYSIS

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Background and Aims:: The timing of endarterectomy after intravenous thrombolysis (IVT) is controversial. Most of literature reports concern IVT and carotid endarterectomy (CEA), while consistent data about IVT followed by other vessels endarterectomy are still lacking; moreover, majority of studies are based on an average interval from IVT to CEA of 48 hours or more.

Methods:: A 32-year old woman, with history of CHT-treated Hodgkin lymphoma, birth control pill assumption, cigarette smoke, was admitted to our ER with sudden left facio-brachial weakness; first examination revealed reduced left arm blood pressure, central facial palsy and distal left arm hypostenia with paresthesias (NIHSS 3). Multimodal CT, including non-contrast CT, angio-CT and penumbral measurement with PCT showed no early ischemic changes involving the MCA territory (ASPECTS 10), signs of hypoperfusion in orbito-frontal and fronto-parietal cortex and brachiocephalic artery stenosis extended to ipsilateral internal carotid artery and right subclavian artery; angio-CT also evidenced left subclavian artery subocclusion.
Results: Immediately after, we administered IV-rTPA, followed by resolution of brachial paresis (NIHSS 2); an echo doppler exam of the epiaortic vessels was performed, showing a floating thrombus in the brachiocephalic trunk. After vascular-surgical evaluation, she underwent brachiocephalic endarterectomy, performed 6 hours after the end of thrombolysis. Post-operative course was uneventful and the patient was discharged with no neurological deficits (NIHSS 0) after 9 days.

Conclusions: This single experience suggests that emergency endarterectomy may be an option in selected patients, to address symptomatic stenosis even immediately after rt-PA therapy (1). NIHSS it’s an
 Brah STROKs in ENVIRONMENTALLY UNFAVORABLE AREAS OF THE ARAL SEA

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Background and Aims:: To study the structure of morbidity and the impact of a set of weather and climate factors on the course and outcome of cerebral strokes in ecologically unfavorable areas of the Aral Sea region.

Methods:: To solve this problem, we analyzed 427 patients with cerebral strokes who were hospitalized in the Khorezm branch of the Republican Scientific Center for Emergency Medical Aid in 2012. Of these, 236 (55.2%) were men, 191 were women (44.8%). The average age of the patients was 57.3 years (56.7 for men and 58.2 for women).

Results:: The study showed that the cause of acute cerebrovascular accident in 58% of cases was hypertension, in 15.2% - atherosclerosis of the cerebral vessels, in 15.8% - a combination of cerebral arteriosclerosis with hypertension. The greatest number of patients was between 60 and 74 years old (43.4%) and from 45 to 59 years (40%), patients with working age (from 20 to 59 years) accounted for 52.6%. Further study showed that hypertension was the cause of brain hemorrhage in 72.3% of cases, subarachnoid hemorrhage of the brain in 64.7%, and cerebral infarction in 55.3%. Atherosclerosis of cerebral vessels mainly caused cerebral infarction in 18.6%, its combination with hypertension was observed with subarachnoid hemorrhage in 23.5%, cerebral hemorrhage in 19.2%, and in cerebral infarction - 14.8%.

Conclusions:: Brain strokes in the Aral Sea region are characterized by a predominance of patients of working age and the main cause of all forms of cerebral strokes is hypertension.
Background and Aims: In acute stroke deterioration of oral function and alteration of consciousness increases the risk of aspiration and pneumonia. Correct oral hygiene and screening for dysphagia is essential to prevent ab ingestis pneumonia that critically increase the days of hospitalization and its long term complications. In our study we compare standardized approach, described in ASA/AHA Guidelines, with a new personalized protocol used in our centre.

Methods: As a first step we carry out a simple swallowing test with a glass of water. If the test is positive, a specialist evaluation is performed which consists of: phoniatric visit, bedside oral exam, flexible endoscopic evaluation of swallowing (FEES) and quantification of the dysphagia degree by 3 clinical scales (Dysphagia Outcome and Severity Scale (DOSS), Penetration Aspiration Scale (PAS), Pooling-score (P-score)); finally, the type of diet and a specific plan of oral hygiene and swallowing rehabilitation are prescribed. In our study we randomized patients into 2 groups: a group treated only with ice chip protocol (ICP) and another group treated with ICP and humidification of secretions with Vapinal. All patients in both groups received basic oral hygiene.

Results: In our study we have demonstrated that an intensive oral hygiene and rehabilitation plan (ICP and Vapinal) guarantees shorter feeding tube durations with faster recovery of oral feeding, improved respiratory function and earlier discharge from the hospital.

Conclusions: In patients with acute stroke and dysphagia an intensive oral hygiene performed by a multidisciplinary approach improve recovery of oral feeding, reduce the days of hospitalization and risk of pneumonia.
RISK FACTORS PROFILE AND CLINICAL OUTCOME OF CARDIOEMBOLIC STROKE PATIENTS ADMITTED IN STROKE CENTER, MONGOLIA

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Background and Aims:: In Mongolia, data on the etiology, risk factors, clinical profile, and outcome of cardioembolic stroke (CES) is scarce and few clinical studies have been performed to date. The aim of this study was to describe risk factors, clinical characteristics, and outcomes of CES in our setting.

Methods:: The case-control study carried out in the Stroke Center and Cardiovascular Center of the State Third Central Hospital for over 7 month period from July 1 2019 to January 31, 2020.

Results:: The study enrolled a total of 525 subjects. CES was detected in 63 (35.7%) out of 176 (33.5%) ischemic stroke patients with a predominance in the age group of 60-69 and men (33%). The main etiology of CES was atrial fibrillation (AF). AF especially paroxysmal AF increased the risk of CES by 4.6 times (p=<0.0001, OR 4.6, 95% CI 1.4-44.6). The main cerebrovascular risk factor was hypertension.

CES involved large volume infarctions and displayed predominantly cortical syndrome (62.2% and 86.5% respectively), while the main clinical signs at onset were sudden onset of maximal deficit (81%), weakness (36.4%), aphasia (18%), and an altered state of consciousness and visual field deficits (10.5%). Neurological deficits assessed by the NIHSS were more severe in men than in women.

Conclusions:: CES accounted for 1/3 of ischemic stroke with substantial morbidity and mortality. The commonest underlying medical conditions were hypertension and non-valvular AF. Hence, all patients with hypertension and non-valvular AF should be meticulously screened for the prevention of CES.
A KOREAN VERSION OF THE OXFORD COGNITIVE SCREEN: VALIDATION STUDY FOR KOREAN HEALTHY GROUP

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Background and Aims:: Cognitive impairment occurs frequently after suffering from stroke and it makes both rehabilitation treatment and returning to work very difficult. And has negative effects on quality of life. Neuropsychological assessment could provide useful information that can be used to assess the extent of post stroke cognitive impairment in order to lead to the accurate diagnosis and proper therapeutic intervention for the patients. This study reports normative data of the Korean version of Oxford Cognitive Screen (OCS-K), a stroke-specific cognitive screening tool.

Methods:: A sample of fifty healthy Korean participants aged 35-79 was assessed using the OCS-K and Montreal Cognitive Assessment (MoCA).

Results:: Mean performance and 5th percentile cut offs were calculated for OCS-K. OCS-K results were similar for results from prior studies Positive and significant correlations found between cognitive subtests in the OCS-K and MoCA indicated good concurrent validity and excellent intra-rater reliability.

Conclusions:: OCS-K including semantics, memory, number writing, praxis, visuospatial, executive functions and orientation will be an optimized tool for cognitive evaluation of stroke patients.
HIGH FREQUENCY OF POST-STROKE SEIZURES AMONG WEST AFRICANS

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Background and Aims: Post-stroke seizures (PSS) are associated with significant morbidity and mortality across the globe. There is paucity of data on PSS in Africa. To assess the frequency and factors associated with PSS by stroke types across 15 hospitals in Nigeria and Ghana.

Methods: We analyzed data on all stroke cases recruited into the Stroke Investigative Research and Educational Network (SIREN). We included adults aged ≥18 years with radiologically confirmed ischemic stroke (IS) or intracerebral hemorrhage (ICH). PSS were defined as acute symptomatic seizures and unprovoked seizures occurring after stroke. We used logistic regression to estimate adjusted odds ratios (aOR) with 95% Confidence Interval.

Results: Among 3,344 stroke patients, 499 (14.9%) had PSS (95% CI: 13.7 – 16.2%). There were 294 (14.1%) PSS among 2091 ischemic strokes and 159 (17.7%) among 897 with ICH, p=0.01. The factors associated with PSS occurrence were age <50 years, aOR of 1.59 (1.08-2.33), National Institute of Health Stroke Score (NIHSS), 1.29 (1.16-1.42) for each 5 units rise and white cell count 1.07 (1.01-1.13) for each 10^3 mm^3 rise. Factors associated with PSS in ischemic were NIHSS score, aOR of 1.17 (1.04-1.31) and infarct volume of 10-30 cm³ aOR of 2.17(1.37-3.45). Among ICH, associated factors were alcohol use 5.91 (2.11-16.55) and lobar bleeds 2.22 (1.03-4.82)

Conclusions: The burden of post-stroke seizures among this sample of west Africans is substantial and may contribute to poor outcomes of stroke in this region. Further longitudinal studies are required to understand the impact on morbidity and mortality arising from PSS in Africa.
AN OBSERVATIONAL ANALYTICAL STUDY OF CEREBRAL COLLATERALS ON COMPUTERIZED TOMOGRAPHIC ANGIOGRAPHY (CTA) IN PREDICTING FUNCTIONAL OUTCOME IN PATIENTS WITH ACUTE ISCHEMIC STROKE IN ANTERIOR CIRCULATION.

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Background and Aims:: BACKGROUND: Good cerebral collaterals restrict the volume of cerebral infarction and improve functional outcome. There are various collateral scoring systems in vogue and this study aims to correlate the relative merits of these scoring systems with functional outcome at three months follow up. Aim To study cerebral collaterals on Computerise Tomographic Angiography in patients with ischemic stroke and classify them using collateral scoring systems. To study the functional outcome in acute anterior circulation ischemic stroke at three months follow up with modified Rankin Scale

Methods:: METHODS: In this prospective observational analytical study patients with acute ischemic stroke in anterior circulation cerebral collaterals were assessed on single phase CTA using MITEFF and MASS scoring systems. Collateral scores were correlated with functional outcome after three months follow up.

Results:: RESULTS: One hundred and four subjects were studied and 62% were males. The mean age was 58±14. Median NIHSS at baseline was 9.5. Good collaterals by MASS (Grade 3-5) were seen in 37% and by Miteff (Grade 3) in 36%. Favourable Outcome was seen in 46%. Using Chi-square test good collaterals were compared between two groups. In Good outcome group 54%had good collaterals by Mass system (p<0.001) and 50% by Miteff System (p<0.05).

Conclusions:: CONCLUSION: In acute anterior ischemic stroke patients with good collaterals by Mass and Miteff system will have good outcome at 3 months.
STRUCTURE OF HEMORRHAGIC STROKES IN YOUNG PEOPLE IN NOVOSIBIRSK (RUSSIAN FEDERATION)

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Background and Aims:: Morbidity among persons under 44 years old is 10% of the total incidence of ischemic stroke and 15% of the total incidence of hemorrhagic stroke. The aim of our study was to estimate the structure of stroke in persons under 45 years old in Novosibirsk, Russia.

Methods:: We analyzed 222 cases of stroke in young people, aged 15 to 45 (mean age 33±15), admitted in the Stroke Unit at the Regional Clinical Hospital (Novosibirsk, Russian Federation) since 01.01.2018 to 31.12.2020.

Results:: There were 42% patients with ischemic stroke (IS) (94 cases), 40% patients with hemorrhagic stroke (HS) (88 cases), 18% with transient ischemic attack (TIA) (40 cases). There was an approximately equal number of subarachnoid hemorrhage (SAH) and intracerebral hemorrhage (ICH) in the structure of hemorrhagic strokes. The main cause of SAH in 85% of cases was rupture of cerebral artery aneurysms, spontaneous hemorrhage in 10%, and in 5% the cause remained undetected. More often, ICH was caused by hypertension or hypertension syndrome (71%), in the second place were vascular anomalies (aneurysm, cavernous angioma, AVM) - 19%, a rare cause (4%) was cerebral sinus thrombosis, in 6% the cause remained unspecified.

Conclusions:: The data of untypical structure of HS can help using a right diagnostic algorithm in young patients
A QUALITY IMPROVEMENT INITIATIVE LOOKING AT OPTIMISATION OF STATIN DOSE IN SECONDARY ISCHAEMIC STROKE PREVENTION AT A TERTIARY STROKE CENTRE

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Background and Aims:: NICE recommend high-intensity statin therapy after stroke to reduce non-HDL cholesterol by >40% by 3 months. No recommendation is provided regarding statin choice or dosage. We aimed to assess the effect of statin choice on lipid profile. The results were used to make recommendations for optimal prescribing.

Methods:: The effectiveness of statins in lowering non-HDL cholesterol in all patients admitted to a HASU over a six-month period was analysed. Categorical data was assessed using the Χ² test and non-parametric data via Mann-Whitney or Kruskal-Wallis. Recommendations were added to discharge summaries requesting GPs to evaluate cholesterol at three months and adjust statin dose. Effectiveness of statin prescribing in all stroke patients presenting to the same HASU over a further one-month period was then analysed.

Results:: In the initial six-month period, 277/310 patients suffered non-haemorrhagic stroke. 55% of these were followed up. 33% of patients on statins achieved >40% reduction in non-HDL cholesterol. All of these were on Atorvastatin with 56% reductions seen at 80mg. All patients on simvastatin had a relative increase in non-HDL cholesterol. Neither failure to measure baseline cholesterol (11%) nor failure to prescribe statin (21-22%) altered across cycles. Atorvastatin prescription was significantly increased in the second cycle (p<0.005) Length of stay was significantly decreased in the second cycle (p<0.0001).

Conclusions:: We propose that Atorvastatin 80mg daily is the most effective lipid-lowering medication. We also recommend including lipid profile blood tests in follow up tertiary review and, if over 40% non-HDL cholesterol reduction is not achieved, to increase to 80mg atorvastatin.
Background and Aims:: Intravenous tissue plasminogen activator (tPA) when administered early to eligible patients with acute ischemic stroke reduces long-term disability and reduces the risks for complications. The international guidelines recommend a door-to-needle (DTN) time to be less than 60 minutes. There are no measured data in our center for DTN times for tPA administration for patients presented with Acute Ischemic Stroke. Hence, our aim is to evaluate DTN times for tPA administrations for patients with acute ischemic stroke before and after the initiation of a quality improvement project.

Methods:: An expert working group in our center developed a quality improvement project after performing a systematic review of the published data on improving DTN times for tPA administration in patients with acute ischemic stroke and identifying protocols and strategies associated with better DTN times. We collected retrospectively all patients presented in our center with AIS and treated with tPA before initiation of the quality improvement project (from September 2018 until October 2019) and 1 year after the initiative (from December 2019 – December 2020).

Results:: Preliminary results showed a significant improvement in DTN times after initiation of the quality improvement strategies. The final analysis will be presented at the conference.

Conclusions:: This single-center quality improvement project was started and showed significant improvement in administrating IV tPA DTN times. We recommend further national strategies for further improvement of tPA administration timelines.
CASE REPORT: ACUTE ISCHEMIC STROKE IN A 15 YEARS OLD FEMALE WITH PATENT FORAMEN OVALE

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Background and Aims:: Patent foramen ovale is a highly prevalent finding in cryptogenic ischaemic stroke, particularly in young adults.

Methods:: We present the case of a 15 year old female patient, previously healthy, with regular sports activity and health check-ups.

Results:: She was admitted due to acute onset of consciousness impairment, left sided hemiplegia, speech impairment, gaze deviation with NIHSS 24 and mRS 5. First brain CT scan performed after 4 hours of the initial treatment was normal. IVT treatment was not provided due to her young age. Laboratory blood and urine analysis, D-dimer, coagulation factors, ECG and extracranial color duplex sonography of the carotid and vertebral arteries were normal. Antiedematous, anticoagulant, antiplatelet, statin and neuroprotective therapy with MLC901 was initiated. Brain MRI 12 hours after initial symptoms showed massive right MCA ischemic stroke in evolution, in nucleus lentiformis, nucleus caudatus and temporal region with surrounding oedema. In the follow-up period, genetic factors for thrombophilia showed heterozygous mutation for F7, F13, ITGA2, PAI-1, MTR, MTHFR 677. TCCS and echocardiography discovered patent foramen ovale, hemodinamically significant, that was treated with percutaneous closure with intracardial prothesis 3 weeks later. Dual antiplatelet therapy with ASA and clopidogrel, as well as statin and neuroprotective therapy with MLC901 was continued. The patient showed dramatic recovery in the follow up period with significantly improved NIHSS, mRS and Short Orientation-Memory-Concentration Test.

Conclusions:: Young patients with stroke should be thoroughly examined for possible risk factors, such as. PFO. MLC901 use was safe and had additional benefit on patients improvement.
Background and Aims:: Acute vestibular syndrome (AVS) features continuous dizziness and may result from a benign inner ear disorder or potentially life-threatening stroke. Misdiagnosis is common and can lead to poor long-term outcome. An oculomotor bedside assessment, the Head Impulse-Nystagmus-Test of Skew (HINTS) is more sensitive than brain Magnetic Resonance Imaging in identifying stroke as the cause of AVS within the first 48 hours, when applied by specialist clinicians. Clinicians’ perspectives of the test in secondary care remains unknown. Here, we explore frontline clinicians’ perspectives of use of the HINTS

Methods:: Clinicians from two large UK hospitals who assess AVS completed a short online survey, newly designed with closed and open questions.

Results:: Almost half of 73 total responders reported limited, or no experience (n=19), reflected in low rates of use (n=31) of HINTS. Whilst the potential utility of HINTS was recognised, many reported concerns about subjectivity, need for specialist skills and poor patient compliance. No clinicians reported high levels of confidence in performing HINTS, with 98% identifying training needs. A lack of formalised training was associated with onward specialist referrals and neuroimaging (p=.044).

Conclusions:: We identified barriers to the application of the HINTS and training needs to improve rapid, cost effective and accurate clinical diagnosis of stroke presenting with vertigo.
ANTITHROMBOTIC PRESCRIPTION AND CLINICAL OUTCOMES AMONG PATIENTS WITH ATRIAL FIBRILLATION IN A RESOURCE LIMITED SETTINGS

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Background and Aims:: Atrial fibrillation (AF) is the most common arrhythmia worldwide and is associated with increased risk of morbidity and mortality. Optimal oral anticoagulation therapy significantly improves the outcomes of patients with AF. We aimed to evaluate the clinical outcomes and their associated factors in patients with AF on antithrombotic therapy in Douala (Cameroon).

Methods:: We prospectively conduct a hospital-based multisite cohort study. Participants enrolled in the Douala Atrial Fibrillation Registry, on antithrombotic treatment were recruited. The composite endpoint of heart failure, stroke, major bleeding, hospitalization and mortality as well as their individual occurrence were assessed 12 months after inclusion in the registry.

Results:: A total of 113 participants were included, and follow-up was completed for 107 of them. The study population was predominantly female (68%), with a mean age of 70 ± 12 years. Antiplatelets were used in 25% of participants and oral anticoagulants in 75% (52% on vitamin K antagonists and 23% on direct oral anticoagulants). At least one outcome occurred in 47.7% (51/107) of cases. Heart failure, stroke, major bleeding, hospitalization and mortality rates were found in 18%, 5%, 3%, 35% and 17% respectively. The mean survival was 11 months. There was no significant difference in the outcomes of patients according to their antithrombotic treatment. Previous heart failure was independently associated with the occurrence of outcomes.

Conclusions:: Three quarter of patients with AF are on oral anticoagulation. About half of the patients with AF will develop an outcome after one year of follow-up, with heart failure being the predicting factor.
EFFECTS OF OUTCOMES (DISABILITY AND APHASIA) OF STROKE ON THE COMMUNITY INTEGRATION OF THE PATIENTS

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Background and Aims:: Stroke commonly results in physical dysfunction and seriously affects the patient’s integration into the community. The aim of this study was to estimate the association of aphasia and disability with the community integration among patients.

Methods:: We investigated the clinical and social aspects of stroke patients. Patients who have undergone ischemic stroke one month ago were assessed with the Modified Rankin Scale (mRS), a severity of aphasia scale and the Community Integration Questionnaire (CIQ). Also, we assayed correlation relationship between these scales.

Results:: Among 141 patients with ischemic stroke, ninety-four patients presented with moderate to severe disability on the Rankin Scale. There was significant negative correlation between CIQ and mRS (p<0.001), and between CIQ and the severity of aphasia scales (p<0.001), indicating lower community integration among people with greater clinical severity of stroke.

Conclusions:: In the present study, the severity of aphasia and disability were inversely correlated with community integration. Improved complex treatment approaches are needed to decrease disability on the social level in these patients.
INTRACRANIAL VERTEBROBASILAR ARTERIAL CALCIFICATION AS A PREDICTOR FOR ISCHEMIC STROKE DUE TO ATHEROSCLEROTIC DISEASE

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Background and Aims:: Intracranial arterial calcification (IAC) has been identified as an independent risk factor for ischemic stroke. The predictive value of calcification severity for the underlying pathophysiological mechanism of an ischemic stroke remains undetermined. We aimed to assess the degree of intracranial artery calcification in patients with ischemic stroke and evaluate its correlation with intracranial artery atherosclerotic disease as the underlying mechanism.

Methods:: Two hundred and eleven patients with strokes attributed to large vessel atherosclerotic disease from the NYU Ischemic Stroke Database, determined by two independent vascular neurologists, were enrolled. Patients with tandem lesions or competing pathophysiologic mechanisms were excluded. Head CT scans for each patient were reviewed. The degree of calcification of each vertebral and basilar artery was determined by two physicians using the Woodcock Score (interrater reliability score of κ=0.88).

Results:: The highest prevalence of calcification was seen in the left vertebral artery (47%), and less commonly in the basilar artery (15%). There was a trend towards higher prevalence of moderate-severe IAC in patients with stroke due to intracranial atherosclerosis than patients with stroke due to extracranial atherosclerosis (40% vs. 28%, P=0.073). The most common risk factors were hypertension (42 vs. 26%, p=0.890), dyslipidemia (25 vs. 19%, p=0.496), and type 2 diabetes (21 vs. 13%, p=0.415), in patients with stroke due to intracranial atherosclerosis vs extracranial atherosclerosis, respectively.

Conclusions:: There may be a positive correlation between the severity of vertebrobasilar atherosclerotic disease as determined by the Woodcock score and the likelihood that the underlying pathophysiological mechanism of an ischemic stroke is intracranial atherosclerotic disease.
Background and Aims:: Poor management of stroke is associated with higher mortality. The present study assessed risk factors for mortality in stroke patients in Kinshasa, Democratic Republic of Congo (DRC).

Methods:: Cross-sectional interviews and clinical assessments were carried out using on 500 subjects [M/F ratio: 1.56; mean (SD) age: 61.4 (±12.3) years] admitted for stroke between 2013 and 2017 in six hospitals in Kinshasa (DRC). Predictors of mortality were determined using logistic regression at 0.05 significance level (STATA software, version 12.1).

Results:: Forty-eight vs. 24% of subjects were admitted for ischemic vs. hemorrhagic stroke, respectively. Median (IQR) time to admission was 48 (78.25) hours. Only 2% of subjects used medical transportation to reach the hospital. Limited expertise in neurology and psychiatry and lack or resources and adherence to treatment protocols were commonplace. Overall mortality reached 32.6%. Predictors of mortality included lack of neurology expertise [OR (95%IC) : 16.6 (6.6-41.7) ; p=0.000], unconfirmed hemorrhagic stroke [OR (95%IC) : 10.3 (4.94-21.5) ; p=0.000], hyperthermia [OR (95%IC) : 5.39 (3.44-8.46) ; p=0.000], hypoxia [OR (95%IC) : 5.13 (3.10-8.47) ; p=0.000], swallowing difficulties [OR (95%IC) : 2.64(1.46-4.79) ; p=0.001], heart disease [OR (95%IC) : 2.53 (1.03-6.17) ; p=0.042], diabetes [OR (95%IC) : 1.72 (1.08-2.74) ; p=0.0023], confirmed hemorrhagic stroke [OR (95%IC) : 1.70 (1.02-2.82) ; p=0.040].

Conclusions:: Neurology expertise with imaging capabilities and control of cardiovascular risk factors may significantly reduce stroke mortality thereby improving stroke outcomes in DRC.
Background and Aims:: We present a case of acute pseudobulbar palsy.
Methods:: A 57-year-old man presented with acute left facial droop and dysarthria. CT brain and CT angiography were negative and antiplatelet treatment was started. Two days later he suddenly worsened and developed anarthria. On neurological examination he was aphonic, but able to answer the questions with signs and writing. He had bilateral lower face and partial left upper face paralysis, his tongue was mildly deviated on the left side with impaired lateral movements. Moreover examination showed poor velum mobility and difficulty swallowing. Ocular motility was spared, rest was normal. Repeated CT and CTA were negative, CT perfusion showed focal hypoperfusion in frontal cortical regions. Brain MRI revealed multiple acute infarcts involving frontal prerolandic and opercular regions bilaterally. Transthoracic and transesophageal echocardiography demonstrated a marantic endocarditis, a condition probably due to hypercoagulable state associated with a newly-diagnosed lung cancer.

Results:: Foix-Chavany-Marie syndrome (FCMS) or bilateral anterior opercular syndrome is the cortical form of pseudobulbar paralysis. It is described as a facio-labio-glosso-pharyngo-laryngo-brachial paralysis with autonomic-voluntary dissociation. The main etiology is the vascular one, consequence of consecutive, multiple, separates vascular lesions in anterior frontal opercula of both hemispheres. Acute onset without a history of previous stroke is unusual. Our case is a rare example of simultaneous bilateral opercular infarcts presenting with acute cortical type of pseudobulbar syndrome.

Conclusions:: In a patient with acute bilateral bulbar signs, preserved ocular motility and absent cerebellar signs should be an alert for a possible cortical site of the lesion, and stroke should be considered as the most likely etiology.
Background and Aims:: Frailty has been identified as an important factor associated with the recovery of various illness, such as: stroke. Therefore, the purpose of this study was to identify the levels of frailty and associated factors for stroke patients after discharged from acute care.

Methods:: A total of 95 stroke patients were recruited and followed up at 3-month and 6-month. Questionnaires included demographic- and medical-information, stroke self-efficacy, and Edmonton frail scale were selected for data collection. All data was managed by SPSS-22. Inferential statistics (i.e. paired-t-test, Chi-Square, multiple logistic regression) were selected to analyze the expected relationship. P<.05 was selected for all analysis.

Results:: Subjects were characterized as: male, lower educated, married, unemployed, living with family members, older, overweight, moderate dependent, and with first or third stroke (33.7% respectively). Most of the subjects were categorized as severe frailty at 3 months and 6 months (37.9% respectively). Meanwhile, the classification of frailty in each sample was the same between 3 months and 6 months. When total score as an issue, the score at 3 months (8.12+3.52) was significantly higher than that at 6 months (6.60+3.13; paired-t=6.283, p<.001). Different predictors for frailty at 3-month and 6-month were found by multiple logistic regression. Marriage_single, ALD_total dependent, ADL_moderate dependent, and self-efficacy were found in both time points.

Conclusions:: Frailty existed in post-discharge stroke patients and improved at 6 months after discharge. Strategies to help the stroke patients manage their frailty need to be explored.
ROLE OF MAGNETIC RESONANCE IMAGING IN IDENTIFYING ACUTE ISCHEMIC STROKE PRESENTING WITH THUNDERCLAP HEADACHE

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Background and Aims:: Acute ischemic stroke represents the most common cause of new sudden neurological deficit. Rapid diagnosis is imperative due to the time-dependent nature of many acute stroke therapies. Thunderclap headache is a severe headache with sudden onset that is often associated with subarachnoid haemorrhage. Here we present a case of ischemic stroke with thunderclap headache at onset that was treated with thrombolysis after urgent brain MRI.

Methods:: We present the case of a 72-year-old woman admitted to our Stroke Unit with sudden onset of severe right temporal headache and vertigo associated with oscillopsia, nausea and vomiting. Her past medical history included palpitations, for which she was taking propafenone. Head CT and CT angiography were negative for parenchymal lesion and no vessel occlusion was found. An urgent perfusion-MRI was then performed showing a DWI restriction of right cerebellum, with corresponding mild FLAIR hyperintensity, as for an hyperacute ischemic injury. Considering favourable mismatch at 3 hours from onset intravenous thrombolysis was administered with marked improvement. At discharge patient had a mild trunk ataxia and was able to walk unsupported.

Results:: In this case prompt brain MRI led to a diagnosis of ischemic stroke in a patient presenting with sudden severe headache, excluding subarachnoid haemorrhage and permitting on time administration of intravenous thrombolysis.

Conclusions:: Thunderclap headache is frequently associated with subarachnoid haemorrhage and is very rarely the onset of an ischemic stroke. Some mimics and chameleons are absolute contraindications to thrombolysis. Urgent brain MRI is sensitive and specific for the diagnosis of ischaemic stroke allowing reperfusion therapy.
SPINAL CORD ISCHEMIA: A RARE MANIFESTATION OF A FLOATING THROMBUS

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Background and Aims:: Spinal cord ischemia (SCI) accounts for less than 1% of all strokes and is often caused by aortic pathologies in the elderly. In this group of diseases, the incidence rate of nonaneurysmal aortic mural thrombus is about 0.45% and the ascending aorta (AA) represents the rarest location. We report a singular case of SCI due to a floating thrombus (FT) in the AA.

Methods:: A 75-year-old male presented to our hospital with acute left hemiparesis and hemihypesthesia, NIHSS 3. His medical history was unremarkable, except for former cigarette smoking. He underwent brain CT and MRI, spinal cord MRI and CT angiography.

Results:: Brain CT and MRI excluded cerebral involvement, while spinal cord MRI showed a C4-C6 ischemic lesion, involving the left anterior and posterior horns of the grey matter and the left lateral cord. A CT angiography demonstrated a 6 millimeter-FT in the AA. According to cardiovascular surgeons, a dual antiplatelet therapy and atorvastatin 80 mg were started. On the 7th day, the patient was discharged with an improvement of his motor deficit, NIHSS 2.

Conclusions:: Although the main symptoms of SCI are often bilateral, the reported clinical features at the onset are exceptionally unilateral. The ischemic lesion may be correlated with an anterior arterial branch occlusion, involving the left spinal sulcal artery territory. Even if the presence of a FT severely increases the risk rate of recurrent embolism (about 73%, compared to 12% of a sessile thrombus), conservative medication is generally preferred.
DOUBLE RISK : STROKE IN A PATIENT AFTER IN VITRO FERTILISATION (IVF) PROCEDURE AND FORAMEN OVALE APERTUM

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Background and Aims:: A major complication of IVF intervention is ovarian hyperstimulation syndrome (OHSS) which can lead to significant arterial and venous thrombosis.

Methods:: We report the case of M.B. a 32 year-old female patient who presented in the Emergency Room in 28 August 2019. She referred that in the morning after the shower she had headache, nausea, vomiting, difficulty speaking and dizziness. She also reported difficulty walking and problems with balance. The situation was aggravated with persisting vomiting and altered consciousness. A head scan was performed and a left cerebellar ischemic lesion was detected. The patient 3.5 years ago consulted an obstetrician and resulted infertile. Then she began a series of more basic hormonal treatments. Has completed a total of 3 FIV cycles within a 2.5 year time frame. (last session April 2019). A complete blood count, coagulation tests, anticardiolipin levels resulted normal. In transesophageal ultrasound was found a foramen ovale apertum. Brain MRI reconfirmed the left cerebellar ischemic lesion, PICA territory. She was given double antiplatelets therapy.

Results:: Ovarian hyperstimulation syndrome (OHSS) remains a serious complication of hormonal treatment among gynecology departments. Haemoconcentration owing to the large fluid shift from the intravascular to the peritoneal cavity results in increased blood viscosity that can lead to arterial and venous occlusion. Thromboembolic stroke, cerebral venous thrombosis and systemic arteriovenous thrombosis have been reported in OHSS.

Conclusions:: Acute ischemic stroke, although much more rare than venous complications, must be considered in a young patient with acute neurological dysfunction and recent ovarian stimulation.
REPERFUSION TREATMENT IN PEDIATRIC ACUTE ISCHEMIC STROKE: A SINGLE-CENTRE EXPERIENCE.

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Background and Aims:: Reperfusion therapy using intravenous thrombolysis with t-PA and / or endovascular treatment significantly improves clinical outcomes in adults with acute ischemic stroke. In pediatric population evidence from randomised controlled trial is lacking, and only case series are available. We describe our experience in pediatric acute ischemic stroke.

Methods:: Single-centre case series of pediatric acute arterial ischemic stroke aged from 2 to 16 years old since 2016 has been examined. Stroke severity was measured with Ped NIHSS (Pediatric National Institutes of Health Stroke Scale). Favorable outcome was defined as 3-month modified Rankin Scale (mRS) less than 2, when applied. Safety measures were intracranial hemorrhage and procedure complications.

Results:: Four cases out of 10 pediatric acute ischemic stroke performed thrombectomy. Nobody received intravenous t-PA. Age was four, nine, ten, and twelve-year-old. Three were female. Two had Down syndrome. Ped NIHSS at onset was 17, 15, 13, and 10. Three intracranial internal carotid artery and one middle cerebral artery occlusion were observed. Complete recanalisation (TICI 3) was obtained in all cases. No intracerebral hemorrhages, neither other procedural complications were observed. Three-month outcome was favorable in all cases (mRS 2, 1, 1, 1, respectively). Extensive diagnostic work-up was carried out to identify stroke etiology. Two had inflammatory arteriopathy, two cryptogenic stroke.

Conclusions:: Although acute treatment of pediatric ischemic stroke is not supported by data from randomised controlled trial, thrombectomy seems effective and safe in pediatric patients, and it could be taken into account in selected cases and in experienced centre irrespective of ischemic stroke etiology.
"LOGOS" IN THE REHABILITATION OF POST-STROKE APHASIA

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**Background and Aims:** According to the national stroke register of 2019 and 2020, more than 60,000 residents in Uzbekistan are diagnosed with strokes every year, and 1/3 of patients have speech disorders-aphasia. The aim is to study the dynamics of aphasia in the acute period of hemispheric strokes and to apply the prototype of the first mobile application in the Uzbek language "LOGOS".

**Methods:** We examined 60 patients with hemispheric strokes from 2018 to 2019. The state of speech functions was studied three times on day 1-3, from day 3 to 21, and in the early recovery period. Group 1 included 28 patients with motor aphasia; group 2 - 12 patients with dynamic aphasia; group 3 - 20 patients with total aphasia. The male sex prevailed, the average age was 64.0 + 1.3.

**Results:** In group 1, speech recovery after 1 day was observed in 7% of patients, within 3-5 days in 7.1%, within 1 week in 14.3%, by the end of the month in 57% and without dynamics in 7.1% of patients. In group 2, dysarthria was mainly detected, speech recovery during the day was noted in 16.7%, within 3 days in 50%, within 5 days in 8.3% and within 1 week in 16.7% of patients. In group 3, speech recovery was noted only in 1 patient.

**Conclusions:** Speech disorders are restored of in the dynamics. The worst recovery is observed in patients with total aphasia. Speech recovery should start with the most acute period of a stroke using the LOGOS mobile speech recovery apps.
GENDER CHARACTERISTICS OF THE MAIN ARTERIES OF THE HEAD

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Background and Aims:: Among the numerous factors, the focus of researchers is on gender differences in both the frequency and clinical features of cerebrovascular diseases. Purpose of the work was an assessment of gender differences in the risk of ischemic cerebral stroke based on the results of a comprehensive ultrasound examination of the main head arteries.

Methods:: The study involved 110 patients aged from 45 to 78 years, divided into two groups: Group I - patients who had an ischemic cerebral stroke in the recovery period (30 men and 22 women), Group II - patients with essential hypertension but no stroke in anamnesis (20 men and 38 women).

Results:: It was found that the average IMT values in the common carotid arteries in men are expected and significantly higher than in women, as in the first (1.10±0.05 mm versus 0.97±0.04 mm, respectively, p<0.05) and in the second (0.87±0.03 mm versus 0.79±0.02 mm, respectively, p<0.05) groups, while significant differences between men and women according to the results of assessing the stiffness of the walls of common carotid arteries were observed in the first group - 8.33±0.22 m/s and 9.16±0.40 m/s, in the second group. Both men and women with uncomplicated hypertension (group II) showed almost the same increase in arterial wall stiffness with an increase in IMT.

Conclusions:: The revealed trend is evidence of qualitative differences in the vessels affected by atherosclerosis in individuals of different sexes and can be used to assess the risk of ischemic cerebral stroke.
THE GENDER FEATURES AND SEASON RELATED ISCHEMIC STROKE AND ITS FREQUENCY

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**Background and Aims::** The aim of the study was to study the seasonal prevalence of ischemic stroke, taking into account its type, gender and deaths.

**Methods::** The analysis included 3112 case histories of patients who are admitted to the TMA clinic. Among them, 1411 are men and 1701 are women.

**Results::** Depending on the month of the year, the maximum prevalence of IS in men was noted in April, and in women - in January (10.9 and 9.9%, respectively). The minimum prevalence of IS was found in men in January, and in women in November (6.3 and 7.0%, respectively). Depending on the season, the prevalence of CS had certain patterns and characteristics. In men, the maximum number of IS cases was noted in summer, and the minimum in winter (28.4 and 21.7%, respectively). In women, if AI is evenly distributed across all seasons of the year. Depending on the type of stroke and gender, certain patterns in the prevalence of deaths at different times of the year were also identified. In men with IS, the maximum number of deaths was noted in the spring, and the minimum - in the summer (32.2 and 16.9%, respectively). In women with IS, the maximum number of deaths was observed in the fall, and the minimum in the summer (30.1 and 20.5%, respectively).

**Conclusions::** AI in men was most often recorded in summer, while in women, its distribution was even throughout the year. The maximum number of deaths with IS was found in spring and fall among men and women respectively.
MINOR STROKE CAN CAUSE MAJOR DISABILITY: IDENTIFICATION OF POOR PROGNOSIS FACTORS IN PATIENTS WITH MINOR STROKE.

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Background and Aims:: Previous studies warn about potential poor functional outcome at three months in minor stroke (MS) patients. Our study aims to ascertain the proportion of patients with poor functional outcome or death at 3 months in this subgroup and to identify factors related to it.

Methods:: A prospective cohort of patients with MS (defined as score in the National Institute of Health Stroke Scale (NIHSS) ≤4), admitted in an acute stroke unit from January 2015 to April 2019 was analyzed. Descriptive and uni-multivariate analyses were performed to identify predictive factors of poor functional outcome or death (defined as a score on modified Rankin Modified Scale (mRS) of 3-6).

Results:: 1048 patients were included, 59% males, mean age 69 years (SD 14.54), median baseline NIHSS 2 (IQR 1-3). 126 (12%) large vessel occlusion (LVO) were identified, acute reperfusion treatment was used in 43 patients (36 intravenous thrombolysis, 11 mechanical thrombectomies). 130 (12.4%) scored mRS>2 at 3 months. Age: OR (1.04 [CI 95% 1.02 - 1.06]), baseline NIHSS: OR (1.4 [1.16 - 1.67]), baseline glycemia >155mg/dl: 1.36 (1.03 - 1.86), LVO: 2.18 (1.26 - 3.76), aterothrombotic etiology: 3.07 (1.55 - 6.09), hemorrhagic transformation: 14.28 (2.31 - 88.28), early recurrence: 15.70 (3.04 - 81.08) and pneumonia: 5.94 (1.82 - 19.40) were identified as predictors of poor outcome in the multivariate analysis (adjusted for age, baseline NIHSS and baseline mRS)

Conclusions:: 12% of MS had poor functional outcome at 3 months. Identifying predictors of poor prognosis could have implications in the initial therapeutic management of these patients.
Background and Aims:: Routine examinations for patients with stroke include clinical assessment using the National Institute of Health Stroke Scale (NIHSS). Although this score accurately predicts the outcome of stroke, the NIHSS is weighted for anterior circulation. No reliable clinical assessment tool has been established for predicting the functional outcome of posterior circulation ischemic stroke. We aimed to develop a stroke scale based on clinical assessment that can increase the yield of detection of posterior circulation ischemic strokes in acute settings, the Langone Augmented Posterior-fossa Stroke Scale (LAPSS).

Methods:: A retrospective, dual campus, single center record review of patients that have been diagnosed with posterior fossa circulation strokes between 12/2018-11/2019 will be conducted. We will catalog the presenting symptoms, calculate their prevalence, and use this information to adjust the current proposed LAPSS. The validity of the LAPSS will then be tested by retrospectively applying it to all patients that presented with symptoms of posterior fossa ischemic strokes.

Results:: We project 120 patients will fit the inclusion criteria. The sensitivity, specificity, positive predictive value, and negative predictive value of LAPSS will be calculated. Inter-rater reliability will be assessed using ANOVA to define an intraclass correlation coefficient. Primary clinical outcome in patients with suspected posterior fossa stroke will be independent functional outcome (mRS 2).

Conclusions:: The NIHSS has been shown to detect <60% of posterior circulation strokes in previous studies. We anticipate that the LAPSS will increase the sensitivity of the NIHSS to increase the overall yield of detection of posterior circulation strokes.
Background and Aims:: A gender gap has been frequently described in stroke care in various settings. We reviewed the issue using data from the admission registries of two our "Stroke Units", located in two distinct Italian regions. Our common policy is to admit every suspected case of acute stroke or TIA to our Stroke Unit, without any specific age or severity-based exclusion criteria.

Methods:: From the two registries, we retrieved data on 2020 admissions. We then analysed possible differences based on gender in age, "wrong diagnosis" (i.e. stroke mimics), stroke severity and thrombolytic treatment. We used chi square test for categorical variables and t-test and Mann Whitney test for continuous variables.

Results:: There were 181 available records. Females were 77 (43%) and males 104 (57%). No difference was found between genders in wrong admissions (p=0.8). Females were significantly older than males (mean age 80 vs 76, p=0.025). Stroke severity (measured by NIHSS) was not different between the two groups (p=0.5) Thrombolysis was given to 15 males and 14 females (p=0.5). Only 3 males and 4 females died while in hospital (p=0.4).

Conclusions:: In the daily practice of two different "Stroke Unit" in central Italy (first level emergency hospitals), no gender differences were found in various parameters of care. When the policy is to admit every suspected stroke to the "Stroke Unit" (as recommended by ESO), male and female patients have the same level and type of care.
ECHOCARDIOGRAPHIC FINDINGS AND DIAGNOSTIC ACCURACY OF ECHOCARDIOGRAPHY IN PATIENTS WITH ISCHAEMIC STROKE OR TIA: A SYSTEMATIC REVIEW PROTOCOL

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Background and Aims:: Stroke is a major cause of mortality and disability worldwide. Approximately 20-30 % of ischaemic strokes are consider to be cardioembolic. Cardioembolic strokes are severe, disabling with high rate of early and long-term recurrence. Both transthoracic and transoesophageal echocardiography are crucial tools in evaluation, diagnosis and management of patients with cardioembolic strokes and TIA’s.

Methods:: A systematic review and meta-analysis has been undertaking to identify studies involving patients with ischaemic stroke and TIA undergoing transthoracic or transoesophageal echocardiogram to detect cardiac source of emboli and to determine the diagnostic accuracy of echocardiography.

Results:: Study question: What are the echocardiographic findings and diagnostic accuracy of echocardiography in patients with ischaemic stroke or TIA? Searches: Electronic databases: MEDLINE (Ovid), EMBASE (Ovid), The Cochrane Library, Scopus. Other resources: the reference lists of included studies, citation tracking, hand searching, grey literature indexed in trials registers ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP). From 01. 01. 2000 to the date of the search with no limitations of languages. Types of study to be included: Cross-sectional diagnostic analytical studies will be considered for inclusion. Condition or domain being studied Ischaemic stroke or transient ischaemic attack. Population: Patients of all ages diagnosed with ischaemic stroke or TIA. Index test: Transthoracic and/or transoesophageal echocardiogram. Diagnosis of interest: Echocardiographic detection of source of emboli.

Conclusions:: The systematic review protocol will be published in Prospero register and results of the systematic review will be presented at the conference.
MLC901 IN SUBACUTE POST-STROKE RECOVERY IN THE EASTERN EUROPEAN POPULATION: PRELIMINARY RESULTS OF A MULTICENTRE STUDY.

Anita Anisovska¹, Mariusz Janta², Anna Tomašová³, Slavomír Guťan⁴, Barbora Garajová⁵, Iveta Nikolová⁶
¹Ss. Cyril and Methodius University of Skopje, University Clinic Of Neurology, Skopje, North Macedonia, ²City Hospital, Department Of Neurology, Częstochowa, Poland, ³Hospital with Polyclinic, Department Of Neurology, Levoča, Slovak Republic, ⁴Hospital with Polyclinic, Department Of Neurology, Považská Bystrica, Slovak Republic, ⁵F.D. Roosevelt Teaching Hospital with Policlinic, Department Of Neurology, Banská Bystrica, Slovak Republic, ⁶Agel Clinic, Center of Movement Medicine, Department Of Neurology, Bratislava, Slovak Republic

Background and Aims:: BACKGROUND: A challenge in the field of Stroke Recovery Research is determining the optimal timing to implement interventions. Acute and subacute (<3 months) is a critical time for neural plasticity, hence should be a target for recovery trials. MLC901, a combination of herbal ingredients, has been used to improve recovery after ischemic stroke. AIM: This study aims to assess the safety and potential efficacy of MLC901 in the subacute to chronic phase after Ischemic Stroke in the Eastern European population

Methods:: MATERIAL AND METHODS: The online NeST registry of subjects with Ischemic Stroke given MLC901 prospectively collected clinical data at baseline and month (M) 1 to M3. Outcome measures included for this analysis is the National Institutes of Health Stroke Scale (NIHSS) and side-effects.

Results:: RESULTS: There were one hundred sixty subjects from Slovakia, Macedonia and Poland, with the mean age was 46.7±27.69 years, with 69 (43%) women, 81% have hypertension and started with MLC901 at 71.13±201 days since the time of stroke onset. Mean NIHSS was 12.5 at baseline, 8.5 at M1, 6.7 at M2 and 5.1 at M3. At M3, 61.01% subjects had minor to no stroke compared to 82.51% with moderate to severe at baseline (Figure 1). During the 3 months follow-up, 1 subject (2.5%) reported at least one adverse event. Figure 1. Proportion of Subjects per scoring levels of NIHSS at baseline, Month 1, M2, M3

Conclusions:: CONCLUSIONS: MLC901 in the real-world setting was safe and showed therapeutic potential for post-stroke recovery at subacute and chronic stages in the Eastern European.
REAL-WORLD EFFECTIVENESS OF MLC901 IN SUBJECTS AFTER BRAIN INJURIES IN THE EASTERN EUROPEAN POPULATION: A PRELIMINARY RESULT OF NEUROAID SAFE TREATMENT (NEST) REGISTRY.

Anita Anisovska1, Mariusz Janta2, Anna Tomašová3, Slavomír Guťan4, Barbora Garajová5, Iveta Nikolová6
1Ss. Cyril and Methodius University of Skopje, University Clinic Of Neurology, Skopje, North Macedonia, 2City Hospital, Department Of Neurology, Częstochowa, Poland, 3Hospital with Polyclinic, Department Of Neurology, Levoča, Slovak Republic, 4Hospital with Polyclinic, Department Of Neurology, Považská Bystrica, Slovak Republic, 5F.D. Roosevelt Teaching Hospital with Policlinic, Department Of Neurology, Banská Bystrica, Slovak Republic, 6Agel Clinic, Center of Movement Medicine, Department Of Neurology, Bratislava, Slovak Republic

Background and Aims:: BACKGROUND: Neurological disorders account for a large and increasing health burden worldwide. MLC901 is a combination of natural products that has demonstrated its clinical efficacy and safety in improving functional and neurological outcomes in stroke, traumatic brain injury, and other neurological conditions. AIM: This study aims to assess the real-world effectiveness of MLC901 in relevant neurological disorders included on the NeST Registry amongst the Eastern European population

Methods:: MATERIAL AND METHODS: Thirty-six physicians from Poland, Macedonia and Slovakia had to enrolled subjects having suffered a brain injury and who were given MLC901 for 3 months. Clinical data were prospectively collected at baseline and month (M) 1 to M3. Outcome measures included National Institutes of Health Stroke Scale (NIHSS), Glasgow Coma Scale (GCS), modified Rankin Scale (mRS) and Short Orientation-Memory-Concentration Test (SOMCT).

Results:: RESULTS: Two hundred six patients were included on this analysis. The mean age was 58.4±14.6 years, 55% are male, and majority have hypertension (76%). Ischemic Stroke accounted for 78% (160/206), Intracranial Hemorrhage (9%), Global Ischemia (6%), and Traumatic Brain Injury (5%). At month 3 (Table 1), mean scores were: 5.87±6.87 (NIHSS), 1.9±1.5 (mRS), 14.13±2.01 (GCS), 14.40±11.24 (SOMCT); with greater proportion of patients improving their mean scores from baseline (Figure 1). Table 1. Baseline characteristics and evolution of scores on neurological scales
Figure 1. Proportions of subjects per scoring levels of four neurological scales at baseline, month (M) 1, M2 and M3.

<table>
<thead>
<tr>
<th>Country Enrolment</th>
<th>CEE NeST (N=206)</th>
<th>Mean (SD)</th>
<th>Median (IQM)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macedonia</td>
<td>Macedon</td>
<td>55 (27%)</td>
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<tr>
<td>Poland</td>
<td>Poland</td>
<td>37 (18%)</td>
<td></td>
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<tr>
<td>Slovakia</td>
<td>Slovakia</td>
<td>114 (58%)</td>
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<table>
<thead>
<tr>
<th>Age in years (yrs)</th>
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<th>Mean (SD)</th>
<th>Median (IQM)</th>
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<tr>
<td>0-19</td>
<td>3 (1.46)</td>
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<td></td>
</tr>
<tr>
<td>20-44</td>
<td>37 (17.96)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-54</td>
<td>32 (15.53)</td>
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<tr>
<td>55-64</td>
<td>48 (23.30)</td>
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</tr>
<tr>
<td>65-74</td>
<td>54 (31.07)</td>
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<tr>
<td>75-84</td>
<td>19 (9.22)</td>
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<tr>
<td>85+</td>
<td>3 (1.46)</td>
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<table>
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<th>CEE NeST (N=206)</th>
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<th>Median (IQM)</th>
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<tbody>
<tr>
<td>Female</td>
<td>93 (45%)</td>
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</tr>
<tr>
<td>Male</td>
<td>113 (55%)</td>
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<th>Comorbidities</th>
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<tbody>
<tr>
<td>HTN</td>
<td>167 (76%)</td>
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<tr>
<td>DM</td>
<td>38 (18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>81 (39)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>35 (17)</td>
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<thead>
<tr>
<th>Onset to Treatment (days)</th>
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<th>Mean (SD)</th>
<th>Median (IQM)</th>
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<tbody>
<tr>
<td></td>
<td>35.7 (20.0)</td>
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<thead>
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<tbody>
<tr>
<td>Ischemic Stroke</td>
<td>160 (78%)</td>
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<tr>
<td>Intracranial Hemorrhage</td>
<td>18 (9%)</td>
<td></td>
<td></td>
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<tr>
<td>Traumatic Brain Injury</td>
<td>10 (5%)</td>
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<td></td>
</tr>
<tr>
<td>Global ischemia</td>
<td>12 (6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>7 (3%)</td>
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<th>Median (IQM)</th>
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<tr>
<td>Baseline</td>
<td>12.64 ± 8.39</td>
<td>12 (0-38)</td>
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</tr>
<tr>
<td>M1</td>
<td>9.29 ± 7.32</td>
<td>8 (0-37)</td>
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</tr>
<tr>
<td>M2</td>
<td>7.72 ± 7.56</td>
<td>5 (0-38)</td>
<td></td>
</tr>
<tr>
<td>M3</td>
<td>5.87 ± 6.67</td>
<td>4 (0-42)</td>
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<thead>
<tr>
<th>mRS</th>
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<th>Median (IQM)</th>
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<tr>
<td>Baseline</td>
<td>3.2 ± 1.45</td>
<td>4 (0-5)</td>
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</tr>
<tr>
<td>M1</td>
<td>2.7 ± 1.4</td>
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<tr>
<td>M2</td>
<td>2.3 ± 1.4</td>
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<tr>
<td>M3</td>
<td>1.9 ± 1.5</td>
<td>2 (0-5)</td>
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<tr>
<td>Baseline</td>
<td>12.52 ± 2.89</td>
<td>15 (3-15)</td>
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</tr>
<tr>
<td>M1</td>
<td>13.58 ± 2.3</td>
<td>15 (3-15)</td>
<td></td>
</tr>
<tr>
<td>M2</td>
<td>13.50 ± 2.11</td>
<td>16 (3-15)</td>
<td></td>
</tr>
<tr>
<td>M3</td>
<td>14.13 ± 2.01</td>
<td>17 (3-15)</td>
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<tr>
<th>SMACT</th>
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<th>Median (IQM)</th>
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<tr>
<td>Baseline</td>
<td>16.91 ± 11.21</td>
<td>20.5 (9-28)</td>
<td></td>
</tr>
<tr>
<td>M1</td>
<td>15.5 ± 10.7</td>
<td>26 (9-28)</td>
<td></td>
</tr>
<tr>
<td>M2</td>
<td>14.99 ± 10.84</td>
<td>16 (9-28)</td>
<td></td>
</tr>
<tr>
<td>M3</td>
<td>14.40 ± 11.24</td>
<td>16 (9-0)</td>
<td></td>
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</table>
Conclusions: CONCLUSIONS: MLC901 in the real-world setting showed therapeutic potential for neurological disease in the Eastern European population.
FEATURES OF THE CLINICAL COURSE OF ISCHEMIC STROKE IN POSTCOVID PATIENTS

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Tashkent Medical Academy, Neurology, Tashkent, Uzbekistan

Background and Aims:: The study of the course of the disease in patients previously ill with COVID-19 infection would contribute to adjusting approaches to the treatment of such patients in order to improve the efficiency of the cure.

Methods:: We observed 45 patients previously ill with COVID-19 and admitted with a diagnosis of ischemic stroke and apply the SF-36, MOCA, HADS, Rivermide, Rankin and NIHSS scales. Of these, 44.4% (20) were women, and 55.6% (25) were men. The average age of patients was 61.2 (52-74) years. The control group of patients, also with ischemic stroke, but without Covid-19 disease in anamnesis, also consisted of 45 people, 48.9% (22) were women and 51.1% (23) were men. The average age of patients was 62.8 (53-78) years.

Results:: In 42 patients previously ill with COVID-19, significant results of the studied indicators indicating a more severe course of the disease were observed compared to those in the control group. At the same time, no significant differences were observed among men and women. In the group of patients who had not previously suffered from COVID-19, only 6 patients (13.3%) also suffered from the disease. The majority of these patients were men aged 63 and above.

Conclusions:: The results of the studies indicate a strong influence of the fact of the previously suffered infection COVID-19 on the nature and duration of the course of ischemic stroke. A history of COVID-19 should contribute to the revision of treatment tactics and the intensity of interventions and be prepared for a longer process of rehabilitation procedures.
ASSOCIATION OF MAJOR ADVERSE CARDIOVASCULAR EVENTS IN STROKE PATIENTS WITH CARDIAC WALL MOTION ABNORMALITIES

Saadat Kamran¹, Naveed Akhtar², Rajvir Singh³, Jon Perkins²
¹Hamad General Hospital, Neuroscience, Doha, Qatar, ²HMC, Neuroscience, Doha, Qatar, ³Heart Hospital, Cardiology, doha, Qatar

Background and Aims:: The association of cardiac wall motion abnormalities (CWMAs) in stroke patients with major adverse cardiovascular events (MACE) remains unclear. The purpose of this study was to estimate the 50-month risk of MACE, including stroke recurrence, acute coronary events and vascular death in stroke patients with CWMA.

Methods:: We performed a retrospective analysis of prospectively collected stroke data over a 50-month period by electronic medical records. Data included demographic, clinical, vascular imaging and echocardiography data including CWMA and MACE.

Results:: Out of a total of 2653 acute stroke patients, CWMA was observed in 355 (13.4%). In CWMA, embolic stroke of undetermined source (ESUS) (50.7%) was the most frequent index stroke subtype and stroke recurrences (p=0.001). In multivariate cox regression after adjustment for demographics, traditional risk and confounding factors CWMA was independently associated with higher risk of MACE (aHR 1.74(95% CI 1.37-2.21), p=0.001). Similarly, CWMA independently conferred an increased risk for ischemic stroke recurrence (aHR 1.50(95% CI 1.01-2.17), p=0.04), risk of acute coronary events 2.50(1.83-3.40), p=0.001) and vascular death (aHR1.57(95% CI 1.04-2.40), p=0.03), in comparison to the stroke patients without CWMA.

Conclusions:: In a multiethnic cohort of ischemic stroke with CWMA, CWMA are associated with 1.7-fold higher risks of MACE independent of established risk factors. ESUS was the most common stroke association with CWMA. Stroke patients should be screened for CWMA to identify patients at higher risk of MACE.
INCREASED CEREBRAL VENOUS SINUS THROMBOSIS DURING COVID-19 LOCKDOWN

Saadat Kamran¹, Naveed Akhtar², Fatma Ben Abid², Muna Almaslaman², Jon Perkins²
¹Hamad General Hospital, Neuroscience, Doha, Qatar, ²HMC, Neuroscience, Doha, Qatar

Background and Aims:: During the Coronavirus Disease-2019 (COVID-19) pandemic, reports of increased cerebral venous thrombosis (CVST) have appeared. Few studies have compared the rate of CVST admissions during the outbreak to previous years. It is not known if preventative measures such as lockdowns affect the rate of CVST presentation.

Methods:: A retrospective analysis of CVST admissions from January 1st, 2019 to December 31st, 2020 was carried out by reviewing the electronic database. All CVST with radiological confirmation were included.

Results:: There was a 13.2% increase in CVST in 2020 compared to 2019 (43.4% vs. 56.6%). CVST was higher during the lockdown period (March to September) compared to the rest of 2020 (p<0.001). This finding could not be replicated in 2019. CVST cases during lockdown remained statistically higher than cases in the rest of 2020 even after removing all COVID-19 cases (34.2% vs. 65.8%, p<0.006). During the lockdown period, the incidence of CVST was 4.0 per 100,000 COVID-19 cases.

Conclusions:: There were more CVST during the lockdown in 2020 compared to the same period in 2019. Lifestyle modifications resulting from lockdown may harmfully impact CVST independent of COVID infection.
ASSOCIATION BETWEEN PLASMA OSMOLALITY AND CASE FATALITY WITHIN ONE YEAR FOLLOWING SEVERE ACUTE ISCHEMIC STROKE

Meng Liu¹, Lun Deng¹, Yajun Cheng¹, Simiao Wu², Long Hao¹, Ming Liu²
¹Sichuan University, West China Hospital, Department Of Neurology, sichuan province, China, ²West China Hospital, Sichuan University, Neurology, Chengdu, China

Background and Aims:: Plasma osmolality, one of the markers of dehydration, is associated with cardiovascular mortality. We aimed to investigate whether elevated plasma osmolality is associated with case fatality within one year following severe acute ischemic stroke.

Methods:: We included severe ischemic stroke patients (defined as National Institutes of Health Stroke Scale ≥15 score) within 24 hours from symptom onset admitted to the Department of Neurology, West China Hospital between January 2017 and June 2019. Admission plasma osmolality was calculated using the equation 1.86*(sodium + potassium) + 1.15*glucose + urea +14. Elevated plasma osmolality refers to plasma osmolality >296mOsm/kg, which indicates a status of dehydration. The outcomes included 3-month and 1-year case fatalities. Multivariable logistic regression was performed to determine the independent association between plasma osmolality and case fatalities at different time points.

Results:: A total of 265 patients with severe acute ischemic stroke were included. The mean age was 71.2±13.1 years old with 51.3% being males. Among the included patients, case fatalities were 31.7% (84/265) at 3 months and 39.6% (105/265) at 1 year, respectively. Elevated plasma osmolality (dehydration) was associated with 3-month case fatality (1.98, 95% CI 1.07-3.66, P=0.029) but not 1-year case fatality (OR 1.51, 95% CI 0.84-2.72, P=0.165) after fully adjustment for confounding factors.

Conclusions:: Elevated plasma osmolality was independently associated with 3-month case fatality but not 1-year case fatality for severe acute ischemic stroke.
REVISITING THE CLASSICS: MIDBRAIN STROKE PRESENTING AS A WEBER SYNDROME

Rafaela Evangelista1, Ana Gomes2, Pedro Ribeiro2, Ilídia Carmezim2, Lénea Porto2, Aline Osuna2, Filipe Blanco3, Rui André2, Vera Ermida1, Bruno Lopes1, David Coutinho1, Elisa Moreira1, Andreia Silva1, Pedro Teixeira1, Jorge Caldas1, Ana Lemos2
1Tondela-Viseu Hospital Center, Physical Medicine And Rehabilitation Department, Viseu, Portugal, 2Tondela-Viseu Hospital Center, Medicine Department, Viseu, Portugal, 3Tondela-Viseu Hospital Center, Neurology Department, Viseu, Portugal

Background and Aims:: Pure midbrain infarcts are rare. Knowledge of the complex neuroanatomy of this region is key to understanding the varied spectrum of disease. We report a patient with well-recognizable Weber syndrome and remarkable imaging correlation.

Methods:: A case report and review of the literature.

Results:: A 73-year-old woman with hypertension, dyslipidemia and class II obesity, presented to the emergency department with a pupil-sparing III right cranial nerve palsy and grade 2 (Medical Research Council (MRC) scale) contralateral hemiparesis. The remaining neurological examination was normal. Thrombolysis was not performed, since it was a wake-up stroke. Initial head CT scan was negative for acute intracranial hemorrhage or ischemia. Head CT angiography excluded large vessel occlusion or relevant focal stenosis. A head MRI revealed a right anterior paramedian mesencephalic hyperintense T2 lesion, with restricted diffusion, suggesting a recent ischemic lesion (Figure 1). Transthoracic echocardiogram excluded structural pathology or intracardiac thrombi. Telemetry monitoring excluded dysrhythmias. After participating in a six-week rehabilitation program, she progressed to grade 4 (MRC scale) left hemiparesis (able to walk), maintaining III right cranial nerve palsy (Figure 2).
Conclusions: Distinguishing between classic midbrain syndromes can prove to be a diagnostic challenge even for skilled physicians. It is our belief that this report is of interest, showing the importance of a guided neurological examination, thorough understanding of neuroanatomy and advanced neurovascular imaging for lesion localization. Although significant improvement of the hemiparesis has occurred, recovery from a nuclear/fascicular palsy of the third cranial nerve is limited and has worse functional prognosis.
SEVERE REFRACTORY REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME: THE OPTION OF INTRA-ARTERIAL VASODILATORS

Sean Freeman¹, Nicolas Bricout², Nelly Dequatre-Ponchelle¹, Charlotte Cordonnier³, Laurent Puy¹
¹University of Lille, Inserm, CHU Lille, U1172 - Lilncog - Lille Neuroscience & Cognition, Lille, France, ²CHRU de Lille, Interventional Neuroradiology, Lille, France, ³Lille university hospital, Neurology & Stroke Centre, Lille, France

Background and Aims:: Reversible cerebral vasoconstriction syndrome (RCVS) is a cerebrovascular disorder associated with multifocal arterial constriction and dilation. Given the lack of data, the management of RCVS is challenging especially for medically refractory forms. We report the case of a 59-year-old woman with severe RVCS complicated by ischemic stroke and diffuse cerebral hypoperfusion despite optimal medical treatment. Combined endovascular infusion of nimodipine and milrinone was beneficial for the patient's radiological and clinical outcomes, suggesting that dual chemical angioplasty is an interesting option in medically refractory RCVS.

Methods:: Following clinical deterioration after optimal medical treatment, we opted for intra-arterial vasodilatory treatment. DSA revealed severe bilateral multifocal vasoconstrictions of the intracranial arteries. A 50 mL syringe containing 6 mg of nimodipine (0.2 mg/mL) and 8 mg of milrinone (1 mg/mL) diluted in isotonic saline solution was prepared for chemical angioplasty. Endovascular application of nimodipine and milrinone was equally distributed in each internal carotid artery by an infusion pump for 15 minutes at an infusion rate of 100 mL/hour. Mean arterial pressure was maintained with adjunct administration of noradrenaline.

Results:: The patient presented gradual neurological improvement in our stroke unit by recovering normal mentation and demonstrated only right-sided brachiofacial hemiplegia and minimal aphasia. CT angiography before discharge showed no irregularities of the intracranial arteries.

Conclusions:: The patient reported a reduction in headache severity and the neurological deficit improved dramatically after therapeutic IADSA. Although the efficacy of endovascular treatments will require further investigation, the use of intra-arterial therapy could be considered in severe and medical refractory RCVS cases.
Background and Aims: Reversible Cerebral Vasoconstriction Syndrome (RCVS) associated with drug treatment has rarely been reported in aplastic anemia. We report a case of drug naive aplastic anemia patient presenting with RCVS.

Methods: Case report of a 50 year old lady with pancytopenia and RCVS who on subsequent evaluation was diagnosed to have aplastic anemia.

Results: A 50 year old lady presented with three day history of headache followed by bilateral dimness of vision and right hemiplegia. She had fatigue, tiredness and dyspnea on exertion for past 2 months. She was detected to have pancytopenia with a hemoglobin of 3g/dL. She had received four packed cell transfusions, the last one three weeks back. On admission, she had cortical blindess and right hemiplegia. Hemoglobin was 7g/dL, total leucocyte count was 3000/mm3 and platelet count was 15000/mm3. MRI Brain showed multiple bilateral infarcts involving frontal, occipital areas and external watershed territories of ACA-MCA and MCA-PCA. Hemorrhage was noted in the left parietal area. MRA showed vasospasm involving distal basilar, bilateral middle cerebral and posterior cerebral arteries. A diagnosis of RCVS was made and she was treated with oral nimodpine and magnesium sulphate injection. Bone marrow biopsy was suggestive of aplastic anemia. She was started on antithymocyte globulin and cyclosporine (caution regarding worsening with cyclosporine was explained). Bone marrow transplantation was suggested however due to financial constraints she cannot afford it. A repeat MRA done 3 weeks later showed reversal of vasospasm of basilar artery.

Conclusions: A rare case of RCVS in drug naive aplastic anemia is reported. Multiple transfusions might have been the trigger for RCVS. Fact that steroids and cyclosporine may worsen RCVS is a management challenge.
AI IMPROVES STROKE DIAGNOSIS AND CARE AT A LOW RESOURCE HOSPITAL IN INDIA

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Background and Aims:: Delay in patient arrival and diagnosis due to limited resources and high patient burden is a key challenge in management of stroke cases. A study was conducted at Baptist Christian Hospital (BCH), India which suffers from a well-known lack of resources and specialists. The study tested the effectiveness of AI solutions to assist low-resource hospitals in LMICs with time-sensitive stroke cases. This abstract suggests AI as a means to improve quality and outcomes to enhance the delivery of healthcare.

Methods:: AI solution (qER) was developed to report abnormalities given a non-contrast CT (NCCT). qER compiles findings into a detailed report highlighting abnormalities, indicating affected brain region along with estimated volume for bleeds. These findings coupled with clinical symptoms helps identify stroke. qER was made accessible by integrating with messaging app enabling notification to be sent about critical diagnosis. This platform further helps in administering medication for the patient in a short time.

Results:: Starting from February 2021 until May 2021, 588 patients were treated with the novel AI based workflow described above. We analyzed 104 consecutively selected patients in the month of February. On average, patients presented 4.5 hrs after the onset of symptoms. Compared to before, novel workflow experienced a reduction of 15-60minutes in the diagnosis phase.

Conclusions:: In stroke cases, qER can help reduce diagnosis time and can guide the treating doctors. qER aims to reduce Door-to-Needle time with intervention via instant reports and phone alerts.
Background and Aims:: Recent studies reported the efficacy of mechanical thrombectomy (MT) alone compared to bridging therapy with intravenous thrombolysis in acute ischemic stroke (AIS) with large vessel occlusion (LVO). This investigation focuses on thrombi composition to gain more insights into the issue.

Methods:: Thirty-seven LVO AIS patients (pts.) who were given either bridging therapy or MT, were studied.

Results:: Twenty-three pts. underwent combined treatment and 14 isolated treatment (MT). Recanalization was achieved in all but two pts., with a good outcome in 29 pts. A slight prevalence of white thrombi, with a greater fibrin load and a lower red blood cell (RBC) component was observed, but with an almost overlapping distribution in both procedures. vWF expression was higher in pts. treated with combined treatment, in line with fibrin load. Statistics: both procedures led to a favourable outcome: P<0.001; no association between fibrin load, RBC load and type of treatment, either isolated or combined, was found: P > 0.05 (MWT). A correlation was observed between collateralization and MT: P = 0.037 (χ²T).

Conclusions:: The study reveals the low thrombolytic efficacy of r-tPA and highlights a more pronounced collateralization in the isolated treatment, probably ascribable to lower thrombus porosity. Given the unproven superiority of TM, the results obtained suggest that further studies are required on thrombi as well as additional research on successful thrombolytic treatments also using adjuvant factors such as antiplatelet or anticoagulants agents, at different doses, antibodies neutralizing pro-thrombotic factors, Adamts-13 enzymes and Nets, nanobodies and novel ultrasound.
KNOWLEDGE OF STROKE RISK FACTORS AMONG THE PATIENTS WITH PREVIOUS STROKE OR TRANSIENT ISCHEMIC ATTACK IN A TERTIARY CARE HOSPITAL OF BANGLADESH

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Background and Aims:: Patients of stroke or transient ischaemic attacks (TIA) are at risk of further stroke. Our objective was to study patients admitted with stroke/TIA regarding their knowledge about risk factors for having a new event of stroke/TIA, possible associations between patient characteristics and patients’ knowledge about risk factors, patients’ knowledge about their preventive treatment for stroke/TIA.

Methods:: A questionnaire was used for 200 patients with stroke/TIA diagnoses. We asked 13 questions about diseases/conditions and lifestyle factors known to be risk factors and four questions regarding other diseases/conditions (“distractors”).

Results:: The risk factors that were most often identified by the patients were Diabetes(75.9%), hypertension(83.3%), previous stroke or TIA(81.5%), smoking(85.2%), regular exercise(75.9%), older age(83.3%), overweight(75.9%) and patients with ischemic heart disease (70.4%). Atrial fibrillation and carotid stenosis were identified by less than 50% of the patients. 44.5% of the patients could identify 10 or more stroke/TIA risk factors. We observed that higher age, having a diagnosis of cerebral infarction/TIA, patients residing in urban area, high income group, businessman/retired service holder, family history of cardiovascular disease, past history of stroke / TIA were related to better knowledge of stroke/TIA risk factors. Only 20(9.3%) of the patients who reported anticoagulants and 76(35.2%) of the patients taking antiplatelets marked them as intended for prevention.

Conclusions:: Knowledge about diabetes, hypertension and smoking as risk factors was good, and patients who suffered from atrial fibrillation or carotid stenosis seemed to be less informed about these conditions as risk factors. Individuals with less knowledge should be given special consideration when developing strategies.
THE EFFICACY OF NEWER NEUROPROTECTIVE AGENT EDARAVONE DEXBORNEOL COMBINED WITH ALTEPLASE ON ACUTE ISCHEMIC STROKE

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Background and Aims:: Edaravone Dexborneol, as a newer multi-target neuroprotective agent, was approved to treat patients with acute ischemic stroke (AIS). The study that efficacy of Edaravone Dexborneol combined with thrombolytic agent alteplase on AIS is less at present. Aims: To observe the clinical efficacy and safety of Edaravone Dexborneol combined with alteplase in the treatment of AIS.

Methods:: 80 patients with AIS were divided into control group (n=40, edaravone combined with alteplase treatment) and study group (n=40, Edaravone Dexborneol combined with alteplase treatment), according to random number table method. The National Institutes of Health Stroke Scale (NIHSS) scores, modified RANKIN Scale (mRS) scores, serum tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) levels before and after treatment, hemorrhagic transformation and adverse reactions during the treatment were compared between two groups.

Results:: The total effective rate of the study group was 87.50% (35/40), which was higher than 67.50% (27/40) of the control group (P<0.05). The NIHSS scores, mRS scores, serum TNF-α and IL-1β levels in two groups were significantly reduced after treatment, and those in the study group were lower than those in the control group (P<0.05). The incidence of hemorrhagic transformation of the study group was 2.50%, which was lower than 15.00% of the control group (P<0.05).

Conclusions:: Edaravone Dexborneol combined with alteplase on AIS has definite effect. It can effectively improve the neurological function, inhibit hemorrhagic transformation, and reduce the level of cytokines.
COMBINATION OF BLOOD BIOMARKERS AND STROKE SCALES IMPROVES IDENTIFICATION OF LARGE VESSEL OCCLUSIONS

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Background and Aims:: Acute ischemic stroke caused by large vessel occlusions (LVO) is the main contributor to stroke deaths and disabilities; however, a tool for triaging LVO patients with confidence is yet to be implemented. In this study we combined the measurement of blood biomarkers with stroke severity scales with the aim of evaluating their diagnostic accuracy for LVO identification.

Methods:: 151 patients with suspected stroke, including stroke mimics, TIAs, haemorrhagic, and ischemic strokes were recruited retrospectively. We analysed the plasma levels of a panel of selected biomarkers in LVO vs non-LVO. Diagnostic performance for LVO identification was estimated by using blood biomarkers alone or in combination with NIHSS-derived stroke severity scales.

Results:: Among 151 patients, 31 (20%) were stroke mimics, 16 (11%) had transient ischemic attack, 16 (11%) had hemorrhagic stroke, 23 (15%) had LVO ischemic stroke, 42 (28%) had non-LVO ischemic stroke, and 23 (15%) had ischemic stroke of unknown origin. Multivariable analysis found that combining two blood biomarkers with stroke scales significantly improved LVO prediction, compared to the stroke scales alone (p-value<0.001). The combination of biomarkers with FAST-ED or EMSA scales resulted in the highest diagnostic performance for LVO identification, achieving an AUC of 95% (95% CI 91-100%) or 93% (CI 95% 89-97%), a sensitivity of 91% (95% CI 71-98%) or 86 (95% CI 66-97%), and a specificity of 95% (95% CI 89-98%) or 94% (95% CI 88-98%), respectively.

Conclusions:: The combination of blood biomarkers and stroke scales can provide a simple and highly accurate tool for identifying LVO patients.
OUTCOME OF THROMBOLYSIS WITH TENECTEPLASE IN STROKE: PRELIMINARY EXPERIENCE IN A TERTIARY CARE CENTRE IN NORTH INDIA

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Background and Aims:: Recombinant tissue-type plasminogen activator (rtPA) is the only FDA approved treatment for thrombolysis in acute ischemic stroke. Tenecteplase, a modified form of rtPA has advantages of lesser cost, ease of administration, longer half-life, and greater fibrin specificity.

Methods:: This was a prospective observational study conducted in PGIMER, a tertiary care centre in India, in acute ischemic stroke patients treated with tenecteplase and alteplase from July 2017 to September 2018. The primary outcomes were improvement in NIHSS scores at 24hours and 1week post thrombolysis or at discharge and functional outcome in terms of mRS at 3months. The safety outcomes were symptomatic intracerebral hemorrhage(SICH) and mortality at 3months.

Results:: There were 39 patients who received tenecteplase and 39 patients who received alteplase. 33.3% patients in tenecteplase group and 41% patients in alteplase group had improvement in NIHSS score by ≥4 or improvement to NIHSS 0 or 1 at 7 days after thrombolysis, or at discharge whichever was earlier(OR: 0.72;CI= 0.29-1.81;p=0.320). Excellent outcome (mRS score of 0-1) at 3-month follow-up was seen in 15.8% patients in tenecteplase group and 38.2%patients in alteplase group(OR: 0.30;CI= 0.10-0.92;p=0.03). Functional independence (mRS 0-2) at 3-month follow-up was seen in 31.6% patients with tenecteplase and 44.1% patients with alteplase(OR: 0.58;CI=0.22-1.53;p=0.27). SICH was significantly higher with alteplase than tenecteplase. Mortality at 3months was 31.6% in tenecteplase and 17.6% in alteplase groups(HR:2.15;CI=0.71-6.58;p=0.27), however, the difference was not statistically significant.

Conclusions:: Tenecteplase was almost as effective as alteplase and safer. It stands as a potential solution for many barriers in thrombolysis especially in resource-limited settings.
EVALUATION OF THE "PARTNERSHIP CARE MODEL" ON QUALITY OF LIFE AND ACTIVITY OF DAILY LIVING IN PATIENTS WITH A CEREBROVASCULAR ACCIDENT

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Background and Aims:: Stroke is a chronic disease with high incidence nowadays, constituting a major public health problem. Annually, 15 million people suffer a stroke worldwide. Stroke rehabilitation requires a sustained and coordinated effort from a large team, including the patient, family and friends, physicians, nurses, and etc. Partnership Care Model, increases involvement, motivation and responsibility of people. The purpose of this study was to evaluate the effect of Long-Term Care Program based on the Partnership Care Model on quality of life in patients with Stroke.

Methods:: This study was randomized clinical trial conducted in Bouali hospital at Qazvin University of Medical Sciences, Iran. The sample size for each group was 40. After assessment and recording basic information (demographic variables, care requirements and problems highlighted in the first step of PCM), the program had two phases: (i) an educational partnership meeting; (ii) a follow-up partnership meeting. SS-QOL instrument was used. Data was analyzed using SPSS 17.

Results:: An increasing trend was observed in the mean scores of quality of life of patients in the intervention group (P-value < 0.05). Before the intervention, the difference between the means in the two groups was small and was not statistically significant, but 3 and 6 months after the intervention. A significant difference between drug use and quality of life three months after the intervention (P = 0.012).

Conclusions:: PCM-based programs may increase patients' quality of life, motivation for life, and participation in treatment and care processes. Since health care requires theoretical knowledge and a prescriptive model, the PCM based on partnership care theory is more effective for chronically ill patients.
ANALYSIS OF FACTORS AFFECTING STROKE-ASSOCIATED PNEUMONIA AT MOHAMMAD HOESIN GENERAL HOSPITAL PALEMBANG

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Background and Aims:: Background: Pneumonia is one of the complications that frequently occurs in stroke patients. The incident in stroke patients happens after the first week of stroke and specifically within the first 3 days of hospitalization in 10% of patients and had a highest risk in the prevalence of dysphagia, immobility, loss of consciousness, and severe stroke. Pneumonia in stroke could prolong the hospitalization period, increase the mortality, and increase the cost for medical treatment. Aim: to find out about the risk factor that affects the occurrence of pneumonia in stroke patients.

Methods:: This study is analytic observational with the prospective cohort approach from June - August 2020. The sample consists of ischemic and hemorrhage stroke that fulfill the inclusion and exclusion criteria. This research will observe the occurrence of pneumonia in hospitalized stroke patients from the onset of the third day until the seventh day.

Results:: From a total of 50 subjects, 10 subjects suffered pneumonia. The onset of pneumonia occurred the most are day three until day five with a total of 8 subjects. There are risk factors found to be related to pneumonia are dysphagia (p= 0.003) with OR= 18.6 and A2DS2 score (p= 0.005) with OR= 13.5. In multivariate analysis, dysphagia is the only risk factor that caused the occurrence of pneumonia (p= 0.061) with OR= 9.143 and the probability of 53%.

Conclusions:: Dysphagia is the main risk factor for the occurrence of stroke-associated pneumonia.
ASSOCIATION OF CHANGED SERUM BRAIN BIOMARKERS WITH PERIHEMATOMAL EDEMA AND EARLY CLINICAL OUTCOME IN PRIMARY ICH PATIENTS

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Background and Aims: Perihematomal edema (PHE) following primary intracranial hemorrhages (ICH) affects the patient outcome. Also, serum biomarkers such as S100 calcium-binding protein B (S100B) and glial fibrillary acidic protein (GFAP) have been associated with ICHs outcome. We aimed to investigate the association between these biomarkers and PHE in ICH patients.

Methods: In this cross-sectional study, patients with primary ICH between January 2020 and August 2020 were evaluated. All participants underwent spiral brain CT scans upon admission, and 48 to 72 hours later and quantification of initial hematoma volume was performed. Serum level of Matrix metalloproteinase-9 (MMP-9), vascular endothelial growth factor (VEGF), GFAP, and S100B on admission were measured by enzyme-linked immunosorbent assays. Acute clinical outcome was assessed by the modified Rankin Scale (MRS), national institute of health stroke scale (NIHSS), and ICH score.

Results: Thirty-seven ICH patients (21 patients with a favorable outcome and 16 unfavorable) were studied. Compared with survival patients, non-survivor patients showed a higher serum level of MMP-9, VEGF, GFAP, and S100B (p<0.05). Scores of absolute PHE, edema expansion distance, and PHE growth rate in the non-survivor group were higher than the survivors (p<0.001). The regression model revealed that MMP-9, VEGF, ICH score, and hematoma volume were associated with the PHE growth rate. S100B and ICH score were associated with edema expansion distance.

Conclusions: Our data showed that the serum level of molecular biomarkers was associated with higher PHE volume and PHE scores were higher in non-survival patients, suggesting it may have a pathogenic role in developing PHE after ICH.
FACTORS AFFECTING THE OUTCOME OF DELAYED INTRAVENOUS THROMBOLYSIS (>4.5 HOURS)

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Background and Aims:: Evidence of the intravenous tissue plasminogen activator (tPA) efficacy beyond the 4.5 hours window is emerging. We aim to study the factors affecting the outcome of delayed thrombolysis in patients of acute ischemic stroke (AIS).

Methods:: Data of patients with AIS who received intravenous thrombolytic after 4.5 hours were reviewed including demographics, risk factors, clinical and laboratory data, stroke classification, vascular distribution, evidence of mismatch, treatment type and onset, National Institutes of Health Stroke Scale (NIHSS) score at baseline, 24 hours, 7 days after thrombolysis and before discharge, modified Rankin Scale (mRS) 3 months after discharge & hemorrhagic transformation (HT).

Results:: We report 136 patients treated by intravenous tPA between 4.53 and 19.75 hours of onset with average duration of 5.7 h. Early neurological improvement after 24 hours occurred in 114(83.8%) patients. After intravenous tPA, the average NIHSS significantly decreased from 6 at admission to 3 after 24 hours, 2 after 7 days, and 1 at discharge (p < .00001). Twenty patients (14.7%) had HT. At 90 days, 91 (67%) achieved good outcome (mRS0–2), while 45 patients (33%) had bad outcome (mRS3-6). Age, endovascular treatment, NIHSS, AF, and HT were significantly higher in the bad outcome group. Age (P=0.001, OR:1.099, 95%CI:1.042-1.160) and baseline NIHSS were predictive of the poor outcome (P=0.002, OR:1.151, 95%CI:1.055-1.256).

Conclusions:: Increased age and admission NIHSS may adversely affect the outcome of delayed thrombolysis and narrow the eligibility criteria. Age and baseline NIHSS based stratification of the patients may provide further evidence as regards the efficacy of the delayed thrombolysis.
RECOVERY OF SPEECH AFTER SUFFERING A STROKE

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Tashkent Medical Academy, Treatment, Tashkent, Uzbekistan

Background and Aims:: The aim of this study was to examine the recovery of speech after suffering a stroke.

Methods:: Materials and methods. We studied 28 people who had suffered a stroke in the neurology department at the TMA. After suffering a stroke, the patients were followed up for 6 months, they were divided into 2 groups. Of 28 (100%) patients, 16 (65%) patients underwent individual speech therapy according to the Pimsler method. The remaining 12 (35%) patients underwent rhythmic transcranial magnetic stimulation.

Results:: As a result of speech therapy according to the Pimsler method and rhythmic transcranial magnetic stimulation, an improvement in speech recovery was noted in the first three months, subsequently the effectiveness of the measures carried out for rhythmic transcranial magnetic stimulation significantly improved than with speech therapy. Current results indicate that 16 patients who received rhythmic transcranial magnetic stimulation were more effective. Their speech recovered within 6 months. In 11 of these patients, speech recovered by 88%, in one it recovered by 60%, and in the remaining 2 patients, speech recovered by 76%.

Conclusions:: It was found that in the recovery period of a stroke, aphasia regresses both due to the activation of the zones immediately surrounding the infarction zone or remote areas of the speech dominant left hemisphere of the brain, and due to the compensatory reorganization of symmetrical structures of the right hemisphere (homologues of the speech zones).
PREVALENCE, SEVERITY AND PREDICTORS OF POST-STROKE DEPRESSION IN A PROSPECTIVE COHORT OF JORDANIAN PATIENTS

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1Jordan University of Science and Technology Faculty of Medicine, Neuroscience, Irbid, Jordan, 2United Nations Relief and Works Agency (UNRWA), Health Services, Gaza, Palestinian Territory, Occupied, 3Jordan University of Science and Technology, Clinical Pharmacy, Irbid, Jordan, 4Jordan University of Science and Technology, Faculty Of Medicine, irbid, Jordan

Background and Aims:: Post-stroke depression (PSD) is the most frequent neuropsychiatric complication of stroke, and it is a significant risk factor for poor functional outcomes and lower quality of life. This study aims to assess the prevalence and severity of PSD and its predictors in Jordanian stroke survivors.

Methods:: A prospective study that enrolled 151 patients with ischemic or hemorrhagic stroke, who were admitted to a tertiary teaching hospital. Demographic data, clinical characteristics on admission, and other relevant study variables were collected. Additionally, stroke outcome was represented by one-month modified Rankin score (mRS) and Barthel Index (BI) scores. Depression screening was performed on admission and after one and three months using the PHQ-9 questionnaire. Prevalence of PSD after one and three months was reported. Logistic regression analysis was conducted to evaluate for significant predictors.

Results:: Depression was reported by 15%, 24.83%, and 17.39% of respondents on admission and after one and three months respectively. Severity increased with time as severe depression was found in 0.71%, 2.13%, and 6.52% of respondents on admission and after one and three months respectively. The second and third questions of PHQ-9 questionnaire were most likely to receive high scores. Significant predictors of PSD were having chronic kidney disease, current smoking status, moderate or severe disability (mRS score) at stroke onset, and severe dependency (BI) after one month (p values 0.007, 0.002, 0.014, and 0.031 respectively).

Conclusions:: One in four Jordanian stroke survivors experienced PSD after one month, while PSD severity increased with time up to three months after stroke.
LEFT ATRIAL ENLARGEMENT AND LONG-TERM RISK OF THROMBOEMBOLIC STROKE AFTER ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

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\textsuperscript{1}Sor Clinic, Department Of Cardiology, Ulaanbaatar, Mongolia, \textsuperscript{2}Mongolian National University of Medical Sciences, Department Of Radiology, Ulaanbaatar, Mongolia

Background and Aims:: ST-segment elevation myocardial infarction (STEMI) causes adverse cardiac remodeling, such as left ventricular (LV) and atrial (LA) chamber dilation, which can induce thrombus formation and subsequent ischemic stroke in this patient population. In this study, we evaluated the association between LA enlargement and long-term risk of having ischemic stroke in patients with STEMI.

Methods:: We chose patients with STEMI who have been treated with primary percutaneous coronary intervention. Two-dimensional (2D) echocardiography was used to evaluate LA volume during admission and indexed to body surface area (LAVi). First thromboembolic stroke after index STEMI was chosen for study endpoint. Spline curve estimation was used to evaluate association between LAVi and risk of having thromboembolic stroke.

Results:: A total of 525 patients were chosen (mean age 60±13, male gender 84.8%). Occurrence of thromboembolic stroke was 1.1\% (n=6) during median follow-up of 27 months (IQR 13; 41). Spline curve estimation showed that LAVi more than 35ml/m\textsuperscript{2} is associated with increased risk of having thromboembolic stroke after index STEMI (Figure 1A). Based on this threshold value, patients were divided into 2 groups. Kaplan-Meier estimation revealed that patients who had LAVi more than 35 ml/m\textsuperscript{2} were had significantly lower event free survival rate compared to patients with LAVi less than 35
ml/m^2 (Figure 1B).

Conclusions: The LA enlargement after STEMI is a strong predictor of long-term thromboembolic stroke and patients with LAVi more than 35 ml/m^2 have significantly event free survival rate.
CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS WITH CEREBRAL VENOUS THROMBOSIS IN A TERTIARY CARE CENTRE

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¹Nirmal Hospital, Neurology, Surat, India, ²Narayana Health City, Neurology, Bangalore, India

Background and Aims:: Aim: To study clinico-etiological factors associated with Cerebral Venous Thrombosis (CVT) in adults and to study factors that influence outcomes in our tertiary care centre.

Methods:: Sample size and technique: 1619 patients with symptoms consistent with CVT evaluated for presence of CVT. 90 cases with a confirmed diagnosis of CVT were included after written and informed consent. Inclusion criteria were age > 18 years and confirmed diagnosis CVT. Exclusion criteria were age < 18 years, those who refused consent for enrolment and arterial strokes. Data collection technique and analysis: A predefined proforma was used to collect data which included demographic profile, clinical profile, imaging findings, routine investigations, investigations specific for etiology of CVT. Outcome was assessed at discharge and at 3 months using the modified Rankin Scale (mRS). Descriptive analyses and comparisons were done for various sub-groups. Significance was assessed at 5 % level of significance.

Results:: 1. The percentage of patients with CVT was 5.55%. CVT was more common in males and average age of 69.9% patients was 36 years. 2. The most common clinical features were headache and seizures. Most common risk factors found were Thrombophilia, Hematological disorders, Idiopathic causes. 3. Endovascular treatment was associated with non-inferior outcomes as compared to medical management. 4. 92.2% patients had a good outcome at discharge and 96.7% at 3 months.

<table>
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<th>Clinical Features</th>
<th>Gender</th>
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<td>Female (n=32)</td>
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<td>Altered sensorium (GCS&gt;9)</td>
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<td>11(34.4%)</td>
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<td>7(21.9%)</td>
<td>11(12.2%)</td>
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<td>7(15.6%)</td>
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<td>Sensory deficits</td>
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<td>Papilledema</td>
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<td>14(43.8%)</td>
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</tr>
<tr>
<td><strong>Hematological condition</strong></td>
<td>48.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>7(12.1%)</td>
<td>26(81.3%)</td>
<td>33(36.7%)</td>
</tr>
<tr>
<td>Paroxysmal Nocturnal hemoglobinuria</td>
<td>0(0%)</td>
<td>2(6.3%)</td>
<td>2(2.2%)</td>
</tr>
<tr>
<td>Polycythemia</td>
<td>9(15.5%)</td>
<td>0(0%)</td>
<td>9(10%)</td>
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<tr>
<td><strong>Drugs</strong></td>
<td>7.8%</td>
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<td></td>
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<tr>
<td>OC pills usage</td>
<td>0(0%)</td>
<td>7(21.9%)</td>
<td>7(7.8%)</td>
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<tr>
<td>Peripartum</td>
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<td>4(12.5%)</td>
<td>4(4.4%)</td>
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<td>Vasculitis</td>
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<tr>
<td>SLE</td>
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<tr>
<td>Sjogren’s</td>
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<td>0(0%)</td>
<td>2(2.22%)</td>
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<tr>
<td>Non-specific</td>
<td>2(3.44%)</td>
<td>0(0%)</td>
<td>2(2.22%)</td>
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<tr>
<td><strong>Thrombophilia</strong></td>
<td>69.9%</td>
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</tr>
<tr>
<td>Hyperhomocysteinemia</td>
<td>41(70.7%)</td>
<td>14(43.8%)</td>
<td>55(61.1%)</td>
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<td>APLA</td>
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<td>1(3.1%)</td>
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<td>Lupus Anticoagulant</td>
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<td>2(2.2%)</td>
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<td>Protein C deficiency</td>
<td>1(1.7%)</td>
<td>0(0%)</td>
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<tr>
<td>Protein S deficiency</td>
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<td>Factor V Leiden deficiency</td>
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<td>Anti-thrombin III deficiency</td>
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<td>0(0%)</td>
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<td>Homozygous MTHFR deficiency</td>
<td>1(1.7%)</td>
<td>1(3.1%)</td>
<td>2(2.2%)</td>
</tr>
<tr>
<td>CNS infection</td>
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<td>2(6.3%)</td>
<td>3(3.3%)</td>
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<tr>
<td>Malignancy</td>
<td>2(3.2%)</td>
<td>2(7.1%)</td>
<td>4(4.4%)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>9(15.5%)</td>
<td>5(15.6%)</td>
<td>14(15.6%)</td>
</tr>
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</table>
Conclusions: 1. CVT is a treatable cause of stroke in young with good outcomes with variable clinicoeiological presentations and warrants a high degree of suspicion. 2. Awareness of Endovascular treatment in patients not responding to medical management should be increased.

<table>
<thead>
<tr>
<th>Treatment Modality</th>
<th>Outcome at discharge</th>
<th>Outcome at 3 months</th>
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<tr>
<td></td>
<td>Good</td>
<td>Poor</td>
</tr>
<tr>
<td>Medical only</td>
<td>93.5%</td>
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<tr>
<td>Medical plus Endovascular</td>
<td>83.3%</td>
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<tr>
<td>P value</td>
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</table>
VALUE OF GLASGOW COMA SCALE AS A PREDICTOR OF SURVIVAL AFTER DECOMPRESSIVE CRANIECTOMY FOR MIDDLE CEREBRAL INFARCTION

Dewa Lal, Depal Attanayake
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Background and Aims: Infarctions of the middle cerebral artery territory increases intracranial pressure rapidly due to ischaemic oedema, often requiring surgical decompression. This study evaluates the value of Glasgow Coma Scale as a predictor of the survival following decompressive craniectomy for Infarctions of the middle cerebral artery territory.

Methods: 21 patients who underwent decompressive craniectomy for Infarctions of the middle cerebral artery territory within 24 hours of the incident were included in the study. Patients with age above 60 years, with severe co-morbidities and with GCS of 15 were not subjected to surgery as a unit policy. Survival and disability based on modified Rankin scale (mRS) were analyzed.

Results: Patients were 08 females and 13 males of 32 to 56 years of age. They were stratified into three groups based on the preoperative GCS. None of the 09 patients with GCS 3 – 8 were survived. 04/08 patients with GCS 9 – 12 and 03/04 patients with GCS 13 – 14 were survived. All survivors of GCS 9 – 12 categories had unfavorable outcome (mRS > 4). 03 survivors of the GCS 13 – 14 categories had favorable outcome (mRS < 3).

Conclusions: GCS 9 is the predictive cut off value for survival in our study group. Therefore, considering the poor survival and unfavorable prognosis, cost of care and clinical work load, decompressive craniectomy for the middle cerebral infarction with GCS less than 09 can’t be rationalized.
A COST-BENEFIT ANALYSIS OF MECHANICAL THROMBECTOMY GENERATED VIA A "BRAIN ATTACK" PROTOCOL

John Rothrock, Allison Koutsandreas
George Washington University, Neurology, Washington, United States of America

Background and Aims:: The advent of mechanical thrombectomy for acute ischemic stroke has produced a paradigm shift in our management of stroke. While mechanical thrombectomy per se appears to represent a cost-effective treatment intervention, the cost-benefit associated with implementation of a thrombectomy-relevant "brain attack" protocol is not as well documented. Purpose of research: To examine selected direct costs and clinical outcome associated with routine use of a thrombectomy-relevant brain attack protocol

Methods:: For a period of 1 year (2020) we prospectively evaluated a consecutive series of patients treated according to our institution’s brain attack protocol. We recorded the frequencies with which RAPID CT perfusion, CT angiography (CTA), catheter-based cerebral arteriography and mechanical thrombectomy were performed and calculated the direct costs associated with those procedures. Assuming a number needed to treat (NNT) of 4 to achieve a positive clinical outcome (i.e., functional independence) from mechanical thrombectomy, we calculated the mean direct cost required to achieve a thrombectomy-related positive clinical outcome.

Results:: We evaluated 412 brain attack patients. RAPID CT perfusion and CTA were performed in 189 cases (46%), catheter-based cerebral arteriography in 41 (10%) and mechanical thrombectomy in 23 (5.6%). The associated direct cost totaled $1.027 million. Applying an NNT of 4 to the 23 patients undergoing mechanical thrombectomy, the mean cost of achieving a positive outcome was approximately $170,000.

Conclusions:: By ICER criteria, these findings suggest that aggressive use of a thrombectomy-relevant brain attack protocol may represent a borderline cost-effective intervention for acute ischemic stroke.
CEREBRAL ISCHEMIC EVENTS IN PATIENTS WITH ATRIAL FIBRILLATION TREATED WITH ORAL ANTICOAGULANTS

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National Hospital Organization Okayama Medical Center, Neurology, Okayama, Japan

Background and Aims:: This study aimed to evaluate the cerebral ischemic events in patients with atrial fibrillation treated with oral anticoagulants.

Methods:: We studied 92 consecutive patients with atrial fibrillation (AF) who had acute cerebral ischemic events during oral anticoagulants admitted from January 2015 to July 2019 in our hospital. Corresponding controls (n=13) were selected based on AF patients without cerebral ischemic events more than five years during oral anticoagulants. We examined the age, gender, risk factors (current smoker, hypertension, diabetes mellitus, hyperlipidemia, myocardial infarction, history of stroke, congestive heart failure, renal failure, CHA2DS2-VASc score), and oral anticoagulants.

Results:: 46% cases of acute cerebral ischemic events were treated with non-vitamin K antagonist oral anticoagulants (NOACs). Other cases were treated with warfarin. The percentages of female, history of stroke, congestive heart failure, CHA2DS2-VASc score more than 4, and CHA2DS2-VASc score were significantly higher in cases of acute cerebral ischemic events.

Conclusions:: The percentages of female, history of stroke, congestive heart failure, and high CHA2DS2-VASc score might be associated with acute cerebral ischemic events during oral anticoagulants.
PROGNOSTIC VALUE OF NEUTROPHIL LYMPHOCYTE RATIO IN ACUTE ISCHEMIC STROKE PATIENTS EITHER RECEIVED REPERFUSION THERAPY OR NOT

Amira Mohieyeldeen
faculty of medicine, Neuro-emergency, quesna, Egypt

Background and Aims:: Very few studies have investigated the specific relationship between (NLR) and the short-term prognosis of patients with (AIS) and receiving intravenous thrombolysis. This study aimed to investigate whether a high NLR is associated with a poor outcome in patients with AIS and after receiving r-tPA.

Methods:: This study was prospective and included 50 patients admitted with clinical picture and C.T finding of AIS in the ED at Menoufia University hospital. clinical data for all patient were recorded,CBC test was taken on admission NLR was calculated,Neuroimaging like C.T brain and MRI if available was done.Initial stroke severity was evaluated by (GCS), (NIHSS) score and (mRS) then was re-evaluated later after 24 hours of admission and after one month.

Results:: Among the 56 patients enrolled, the mean age of the study population was 62 (35–90) years,40 patients did not receive rt-PA ,37.5 % of them (15 patients) had a good prognosis . their NLR on admission was 2.9±0.7. And 55% of these patients (22 patients) had abad prognosis . their NLR on admission was 10.1±2.7 on the other side the 16 patients who received r-tPA ,68.7% of them (11 patient) had agood prognosis their NLR on admission was 3.3±1.7 and 31% of these patients (5 patients) had abad prognosis their NLR on admission was7.04±1.1.

Conclusions:: Our results confirm that elevated NLR on the hospital admission is an easy and strong predictor of poor outcomes in AIS patients either receiving reperfusion therapy or not.
DOES GENDER DIFFERENCE MATTER IN CEREBRAL VENOUS THROMBOSIS?

Jayantee Kalita, Usha Misra, Varun Singh

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Background and Aims:: There may be gender difference in clinical, imaging findings and outcome of cerebral venous thrombosis (CVT) because of female specific risk factor (FRSFs). We compare the non-FRSF, clinicoradiological severity and outcome in CVT in males and females, and also compare these parameters in female patients with and without FSRFs.

Methods:: 172 patients were included from a prospectively maintained CVT registry. The diagnosis was based on magnetic resonance venography (MRV). Clinical details, risk factors, MRI and MRV findings were noted. The risk factors in the females were categorized as FRSF only, FSRF in addition to other risk factor, non FSRF only and no risk factor groups. Outcome was defined at 6 months using modified Rankin Scale (mRS) as death, poor (mRS > 2) and good (mRS < 2).

Results:: 80 (46.5%) patients were females; 24 (30%) had FSRFs and 18 (75%) of whom also had other risk factors leaving only 6(25%) females with isolated FSRF. The frequency of other prothrombotic risk factors, clinical and imaging findings were similar in males and females except more frequent hyperhomocysteinemia in males (59% vs 41%; P = 0.036) and altered sensorium in females (66% vs 40%; P = 0.001). 17(9.9%) patients died, 12(7%) had poor and 143(83.1%) had good outcome. The outcomes were similar in both the gender, and in the females with and without FSRF.

Conclusions:: Isolated FRSF is rare in CVT, and there is no gender difference in terms of non FRSFs, clinicoradiological severity and outcome.
MEDIATION EFFECTS OF MEAN HOUNSFIELD UNIT ON RELATIONSHIP BETWEEN HEMOGLOBIN AND EXPANSION OF INTRACEREBRAL HEMORRHAGE

Yong Soo Kim¹, Han-Gil Jeong², Hee-Yun Chae³, Moon-Ku Han¹
¹Seoul National University Bundang Hospital, Neurology, Bundang-gu, Seongnam-si, Korea, Republic of, ²Seoul National University Bundang Hospital, Neurology, Neurosurgery, Bundang-gu, Seongnam-si, Korea, Republic of, ³Chungbuk National University Hospital, Neurology, Cheongju-si, Korea, Republic of

Background and Aims:: Low hemoglobin levels are known to be associated with hematoma expansion (HE) of intracerebral hemorrhage (ICH). However, it is not yet known whether low hemoglobin itself causes HE or is merely a confounder. Thus, we investigated the mediation effect of the mean Hounsfield unit (HU) of hematoma on the relationship between low hemoglobin and HE.

Methods:: Overall, 232 consecutive patients with ICH who underwent non-contrast computed tomography (NCCT) within 12 hours since onset were included. The mean HU and hematoma volume on NCCT were investigated using semi-automated planimetry. The respective associations among the hemoglobin level, mean HU, and HE were analyzed using multivariable regression analysis. Mediation analysis was performed to examine the potential causal association among the three.

Results:: HE occurred in 34.5% of patients; hemoglobin levels were inversely associated with HE (adjusted odds ratio, 0.89; p=0.02). The mean HU of the hematoma was lower in patients with HE than in patients without HE (58.5±3.3 vs. 56.8±3.0; p<0.01). Hemoglobin levels on admission were linearly related to the mean HU (adjusted β, 0.35; p<0.01) after adjusting for known HE predictors. Causal mediation analysis showed a significant mediation effect of the mean HU on the association between hemoglobin levels and HE (p<0.01). The proportion of indirect effect through the mean HU among the total effect was 37% (p=0.04).

Conclusions:: The mean HU of the hematoma fully mediated the association between hemoglobin levels and HE. The mean HU of the hematoma may be a robust marker of impaired hemostasis in patients with ICH.
REVERSIBLE CEREBRAL VASOCONTRACTION SYNDROME IN AMPHETAMINE ABUSE

Karthik Mahesh¹, Chirag Ahuja², Abeer Goel¹, Sukriya Saravanan¹
¹PGIMER, Neurology, Chandigarh, India, ²Postgraduate Institute of Medical Education and Research (PGIMER), Neuroradiology, Chandigarh, India

Background and Aims:: Background & Aims: Substance abuse and overdose are a common cause for morbidity and mortality in young healthy individuals. We describe a patient who presented with acute onset loss of consciousness, following IV amphetamine injection. He was diagnosed as RCVS (Reversible cerebral vasoconstriction syndrome) based on angiogram. He was treated with a course of IV steroids followed by complete recovery over 2 weeks.

Methods:: Methods: We present a case of young male with history IV amphetamine abuse followed by sudden loss of consciousness and seizures. On examination he was comatose GCS of E1M1Vt. The NCCT head revealed multiple intraparenchymal bleed and SAH. The CT angiogram revealed vasospasm of B/L MCA (Middle cerebral artery), VA (Vertebral artery) and Basilar artery. His urine toxicology for Amphetamine was positive. He was given Antiepileptics (Levetracitam 1gm/day) and was given 5 days of IV methylprednisolone 1 gm. The patient gradually improved over a period 1-2 weeks and was weaned of the ventilator and discharged.

Results:: The management of Amphetamine induced RCVS is still challenging. The role of steroids is limited to case reports and series.

Conclusions:: RCVS due to any cause especially amphetamine can be steroid responsive and may alleviate morbidity.
WAKE-UP STROKE (WUS) VERSUS STROKE WITH KNOWN ONSET TIME: CLINICAL AND BRAIN IMAGING CHARACTERISTICS AND TREATMENT OPTIONS

Erum Shariff, Danah Aljaafari, Aishah Albakr, Sari Subaihani, Saeed Aljubran, Noman Ishaque, Reem Alomar, Fahad Alkhamis, Abdulaziz Al-Sharydah, Mohammad Alshurem, Majed Alabdali

1King Fahd Hospital, Imam AbdulRahman Bin Faisal University, Neurology, Alkhobar, Saudi Arabia, 2King Fahd Hospital, Imam AbdulRahman Bin Faisal University, Radiology, Alkhobar, Saudi Arabia, 3King Fahd Hospital, Imam AbdulRahman Bin Faisal University, Community Medicine, Alkhobar, Saudi Arabia

Background and Aims:: To identify clinical and imaging characteristics on admission between WUS patients and awoke stroke patients. To correlate these findings to the possible mechanism of WUS.

Methods:: This is a prospective observational cohort study conducted at King Fahd Hospital of the University includes Acute Ischemic Stroke (AIS) presenting within five days of symptom onset, from April 2017 till March 2019. Patients were grouped into two groups; group 1: Wake-up Stroke (WUS); Group 2: awoke stroke. Comparative and correlative data analyses have been done. Descriptive statistics for continuous data have been reported as medians and interquartile ranges (IQRs) as it is a better representation of skewed data. Categorical data were compared mainly by Chi-squared tests and Fisher's Exact test where numbers were small between cells.

Results:: Among 645 patients, 448 patients fulfilling the criteria of AIS, included in the study. WUS was identified in 112 (25%). Median age was not different among the groups. There was no gender preponderance found between the two groups. Regarding comorbidities; DM, HTN, and Dyslipidemia was high in WUS group, compared to AF, history of stroke and epilepsy was more in awoke stroke group. Bihemispheric stroke was more in awoke stroke group (6% vs 2.7%; p-0.06).

Conclusions:: There were only minor differences between clinical and imaging characteristics of WUS and awoke stroke found. Circadian patterns of stroke onset were observed in all groups, stroke was more likely to occur during waking than during sleep and, in the diurnal period, during morning than during afternoon.
ACUTE IRON OVERLOAD AGGRAVATES BLOOD BRAIN BARRIER DISRUPTION AND HEMORRHAGIC TRANSFORMATION AFTER TRANSIENT FOCAL ISCHEMIA IN RATS WITH HYPERGLYCEMIA

Qian Wu¹, Siqi Guo², Junfeng Liu¹, Hengyi Xiao³, Yanan Wang¹, Yajun Cheng¹-⁴, Simiao Wu¹, Bo Wu¹, Ming Liu¹
¹West China Hospital, Sichuan University, Neurology, Chengdu, China, ²West China Hospital, Sichuan University, West China School Of Medicine, Chengdu, China, ³West China Hospital, Sichuan University, Lab For Aging Research, Center For Medical Stem Cell Biology, State Key Laboratory Of Biotherapy, Chengdu, China, ⁴Sichuan University, West China Hospital, Department Of Neurology, sichuan province, China

Background and Aims:: We aimed to verify whether acute intracerebral iron overload aggravates blood-brain barrier(BBB) damage and hemorrhagic transformation(HT) after transient focal ischemia in rats with hyperglycemia and deferoxamine(DFX) maintains the integrity of BBB and reduces a risk of HT.

Methods:: A hyperglycemia-induced HT model in middle cerebral artery occlusion(MCAO) rats were established. Animals were assigned to four groups: Sham, Vehicle, Iron overload and Iron chelator. Brain samples were collected at 24 hours after surgery to quantify the amount of hemorrhage, determine extravasation of Evans blue and IgG and detect the levels of following proteins: ferritin, metalloproteinase-9(MMP-9), zonula occludens-1(ZO-1), Occludin and Claudin-5 by western blot analysis and immunohistochemistry.

Results:: Compared to the Vehicle group, the Iron overload group had a significantly higher amount of hemorrhage and more extravasation of Evans blue and IgG. The Iron overload group had lower levels of ZO-1, Occludin and Claudin-5 and higher levels of ferritin and MMP-9 than the Vehicle group(all P<0.05). Administering DFX reduced the extension of hemorrhage and extravasation of Evans blue and IgG, reversed the MCAO-induced reduction of ZO-1, Occludin and Claudin-5 and decreased the levels of ferritin and MMP-9.

Conclusions:: Our results suggest that acute intracerebral iron overload aggravates BBB damage and HT after ischemic stroke, which provides evidence of ferritin as a potential biomarker determining iron overload status and predicting for BBB damage and HT. DFX has a remarkable effect of ameliorating iron overload, preserving BBB integrity and reducing HT, which might be a prospective neuroprotective drug for preventing HT after ischemic stroke.
AUTOMATED QUANTITATIVE ANALYSIS OF CEREBROVASCULAR REACTIVITY MEASURED BY ACETAZOLAMIDE SPECT FOR DETECTION OF ABNORMAL CEREBROVASCULAR TERRITORIES

Yeongbae Lee¹, Byungkwan Jung², Chang-Ki Kang³
¹Gil Medical Center, Gachon University College of Medicine, Neurology, Incheon, Korea, Republic of, ²Gachon University, College Of Medicine, Incheon, Korea, Republic of, ³Gachon University, Neuroscience Research Institute, Incheon, Korea, Republic of

Background and Aims:: Acetazolamide (ACZ) SPECT is a useful method to assess reduced brain perfusion but generally relies on subjective visual evaluation. This study quantitatively analyzed the distribution of voxel-based cerebrovascular reactivity (CVR) values to localize and classify the abnormal cerebrovascular territories by their severity.

Methods:: Sixty-seven acute stroke patients (39 males and 28 females) were subject to study, and their age was 39-90 (average 63.3). Nuclear medicine specialists recorded up to 4 brain regions with anomalies in the order of severity. Voxel-based CVR values were analyzed by regions to find out statistical characteristics of normal and abnormal cerebrovascular territories. Then, a machine learning method of Gaussian mixture model was used to differentiate the effects of abnormal microvessels from CVR values of a region.

Results:: Abnormal cerebrovascular territories, selected by nuclear medicine specialists, could be classified into two types (Figs. 1(a) and 1(b)). The CVR values within the first type of lesions (Fig. 1(a)) are lower than normal regions (Fig. 1(c)). In contrast, distribution of the second type of lesions (Fig. 1(b)) is similar to normal regions. Fig. 2 supports the assumption of microvascular abnormality within the second type of lesion. The machine learning could extract abnormal microvessels with low CVR value as shown in red box in Fig. 2(b) and 2(c).

Conclusions:: CVR values of abnormal cerebrovascular lesions could be classified into two groups using a machine learning method. The result suggests that CVR distribution of the second group, similar to normal regions, can occur as a result of abnormal microvessel.
CERVICOMEDULLARY CAVERNOUS HEMANGIOMA PRESENTING AS SPINAL SHOCK SYNDROME AND DYSFUNCTION: A CASE REPORT

Jenielyn Nazaire, Debbie Liquete
Baguio General Hospital and Medical Center, Neuroscience, Baguio City, Philippines

Background and Aims:: Cavernomas are rare congenital benign angiographically occult vascular malformations of brain accounting for 5-15% of all brain vascular malformations. A Cervico-medullary junction location is very rare, with only 8% cases being reported in the literature. This is a case report of a patient who presented with progressive and step-wise deterioration of spinal cord function and spinal shock syndrome. Pressure effects due to changing dynamics in the cavernous malformation resulted in mass effect over the spinal cord level as the possible mechanism. Treatment of patient with cavernous malformations of CMJ requires understanding of its natural history, local neurovascular anatomy including safe entry point to the brainstem, skull base approaches to cranio-vertebral junction and microsurgical techniques unique to its resection. This should be weighed with knowledge of the risks and indications for treatment as surgery itself causes significant morbidity.

Methods:: A case report

Results:: In this case report, the hemangioma was located at the caudal medulla extending to C4 region in the intramedullary location. but this was obscured by blood products at the time of initial imaging, making diagnosis difficult (Figure 1).
Magnetic resonance imaging was done three months after conservative management showing evidence of regression (Figure 3).

**Conclusions:** Cavernomas of brain stem and spine have more dynamic course than supratentorial cavernomas and should be considered for any case presenting as spinal shock and dysfunction. Surgery should be done only when there is appropriate indication, as surgery itself causes significant morbidity.
IMPACT OF THE FIRST STROKE ON PATIENTS AND CAREGIVERS: DEPRESSION PREVALENCE AND PREDICTORS IN A PROSPECTIVE COHORT FROM JORDAN

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¹Jordan University of Science and Technology Faculty of Medicine, Neuroscience, Irbid, Jordan, ²United Nations Relief and Works Agency (UNRWA), Health Services, Gaza, Palestinian Territory, Occupied, ³Jordan University of Science and Technology, Faculty Of Medicine, irbid, Jordan

Background and Aims:: Depression is an important neuropsychiatric complication in stroke survivors. Caregivers are susceptible to increased social and emotional burdens and a high risk for depression.

Methods:: This prospective study included 108 dyads of first-stroke survivors and their caregivers. Demographic data, clinical characteristics and other relevant variables were collected. Stroke outcome was represented by one-month modified Rankin (mRS) and Barthel Index (BI) scores. Depression screening was performed for patients and caregivers on admission and after one month using the self-reported PHQ-9 questionnaire. Changes in prevalence and severity of depression were calculated. Logistic regression analysis was conducted to evaluate for significant predictors of depression in both groups.

Results:: A total of 88 patients responded to both screenings, while 101 and 96 caregivers responded to the first and second screenings, respectively. Depression was reported by 9.09% and 23.87% of patients on admission and after one month, while the prevalence among caregivers was 8.91% and 15.62%, respectively. The increase in the numerical continuous variable for caregiver PHQ9 scores was significant (p 0.022). Significant predictors of patient PSD were the length of hospitalization (P 0.048) and caregiver depression (P 0.034). Predictors of caregiver depression were female caregiver gender (p 0.033), higher patient disability after a month (P 0.004), higher initial stroke severity (P 0.032), and caring for a patient with post-stroke depression (P 0.023).

Conclusions:: Both stroke survivors and their caregivers are at high risk of depression. Early recognition of this complication is important to improve outcomes and mitigate the negative impacts of stroke.
Background and Aims:: About 10- 15%of all ischemic strokes occur in young adults ,limited researches have specifically addressed stroke in the young, also, the etiology of ischemic stroke in the young are heterogeneous and can be relatively uncommon the purpose is to identify different risk factors of stroke in young.

Methods:: consecutive 29 patient with acute ischemic stroke in young adults were admitted to neurology department, Sohag university hospital were compared to elderly group

Results:: prevalence of Rheumatic heart disease is common in young adult ,hypertension is the most prevalent vascular risk factor.

Conclusions:: Rheumatic heart disease still prevalent in young adult in a sample of Egyptian population, hypertension is the most important modifiable risk factor,Scandinavian stroke scale on admission is a predictor of hospital mortality in young adults with acute ischemic stroke.
DYNAMICS OF RECOVERY OF COGNITIVE AND NEUROLOGICAL FUNCTIONS IN PATIENTS WITH PRIMARY AND RECURRENT ISCHEMIC STROKE IN ULYANOVSK REGION.

Rizida Sharafutdinova1, Imil Khairullin2
1Ulyanovsk State, Internal Medicine, Ulyanovsk, Russian Federation, 2Ulyanovsk State University, Internal Medicine, Ulyanovsk, Russian Federation

Background and Aims:: According to WHO statistics repeated strokes develop during the 1st year in 35% of patients and are significantly more likely to lead to disability and death. Aim. To compare degree of impairment and dynamics of cognitive and neurological functions in patients with primary ischemic stroke (IS) in VBB and patients with IS in VBB, having acute cerebral blood circulation disorders.

Methods:: 52 patients aged 39-87 years were examined in the most acute (1 day) and acute (10 days) periods of IS in VBB, 23 of them had primary IS, and 29 patients had acute cerebral blood circulation disorders. Neurological functions were investigated using the NIHSS-scale, CT-data and other laboratory and instrumental methods. Cognitive abnormalities were identified using MMSE and MOCA-test (Mann-Whitney U-test criterion was applied). The differences were considered valid when significance of p<0.05 was significant. The results are presented in form of arithmetic mean and standard deviation (M±s).

Results:: The average age of patients who underwent first IS was 60.87±11.81 years, and average age of patients with repeated IS was 61.62±11.59 years. When analyzing the data, reliable results (p<0.01) were obtained that in acute period of time patients with repeated IS had more pronounced cognitive disturbances and lower dynamics of their recovery than patients who had suffered IS for first time. Also, patients with repeated IS had more pronounced neurological deficits on both 1 day and 10 days than patients with IS for first time.

Conclusions:: Patients with repeated ischemic stroke have more pronounced cognitive and neurological impairments than patients with first time ischemic stroke. In addition, patients with repeated stroke have lower rates of recovery of cognitive and neurological function than patients with primary stroke.
ELECTRIC MYOCARDIAL INHOMOGENEITY AND STROKE: CONNECTION AND SPECIFICS.

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¹Ulyanovsk State, Internal Medicine, Ulyanovsk, Russian Federation, ²Ulyanovsk State University, Internal Medicine, Ulyanovsk, Russian Federation

Background and Aims:: The inconsistency of literature data on influence of different hemispheric localization of Cerebrovascular accident (CVA) on development of cardiac arrhythmias suggests expediency of further study of so-called “zones” of cerebral cortex associated with electrical instability of myocardium. It is known that dispersion of QT interval and fragmented myocardial activity belong to markers of electrical instability of heart and are associated with arrhythmogenesis. Aim of study. To study severity of abnormalities of parameters of electrical instability of myocardium in right and left hemispheric stroke localization in patients with hypertension.

Methods:: 111patients with left hemispheric localization of ischemic stroke and 75patients with right hemispheric stroke were examined. Hemorrhagic stroke was observed in 17patients in left hemisphere and in 13patients in right hemisphere. The average age was58,2±7,48years. For all strokes, men prevailed (64%vs.36%). For first day of stroke, all patients were evaluated for QT dispersion and fragmented myocardial activity on device "Polyspectro-8EX"(Russia).

Results:: Evaluation of the parameters of electrical instability of myocardium in patients with stroke revealed more pronounced disorders in hemorrhagic stroke of left hemispheric localization (Table 1). In ischemic stroke, the severity of electrophysiological parameters, reflecting the instability of the myocardium depending on the hemispheric localization, indicates the absence of differences.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>IS LA (n=111)</th>
<th>IS RA (n=75)</th>
<th>HS LA (n=17)</th>
<th>HS RA (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tot QRS, ms</td>
<td>126.8±13.6</td>
<td>130.2±13.3</td>
<td>137.77±10.4</td>
<td>130.00±3.57</td>
</tr>
<tr>
<td>RMS40, mV</td>
<td>11.5±6.2</td>
<td>16.0±9.9</td>
<td>8.00±3.00</td>
<td>15.33±1.86</td>
</tr>
<tr>
<td>LAS40, ms</td>
<td>51.5±12.2</td>
<td>47.6±15.8</td>
<td>53.55±7.87</td>
<td>41.16±2.85</td>
</tr>
<tr>
<td>QTd, ms</td>
<td>47.1±23.7</td>
<td>47.0±29.8</td>
<td>64.11±24.72¹</td>
<td>30.33±13.12</td>
</tr>
<tr>
<td>QTcd, ms</td>
<td>55.6±24.2</td>
<td>49.37±37.7</td>
<td>66.55±23.48¹</td>
<td>33.66±15.71</td>
</tr>
<tr>
<td>QTcnd, ms</td>
<td>15.83±6.4</td>
<td>16.68±14.0</td>
<td>19.66±6.65¹</td>
<td>10.66±4.41</td>
</tr>
</tbody>
</table>

Conclusions:: Conclusions. 1. The most pronounced disturbances in the parameters of electrical stability of the myocardium is observed in hemorrhagic stroke. 2. The severity of myocardial electrical instability in ischemic stroke is not associated with the localization of the focus.
STRUCTURAL-ELECTRICAL REMODELING OF MYOCARDIUM IN NEUROLOGICAL DEFICITS IN PATIENTS WITH ISCHEMIC STROKE: IS THERE A CONNECTION?

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1Ulyanovsk State, Internal Medicine, Ulyanovsk, Russian Federation, 2Ulyanovsk State University, Internal Medicine, Ulyanovsk, Russian Federation

Background and Aims:: Theoretical and clinical questions of correlation between structural-electrical remodeling of heart and severity of neurological deficits at stroke have not been developed or remain controversial so far. Aim. To study peculiarities of structural-electrical remodeling of myocardium with severity of neurological deficit in patients with ischemic stroke (IS).

Methods:: 111 patients with IS in left and 75 patients in right brain hemispheres were examined. The average age was 56.7 ± 5.58 years. All subjects underwent an ultrasound examination of heart using ALOKA-SSD5000 apparatus (Japan) and QT-dispersion using Polyspectro-8 EX apparatus (Russia). Duration of QT-dispersion interval more than 50 ms was considered pathological.

Results:: Structural remodeling of heart in patients with IS was manifested by prevalence of high values of finite-systolic volume of LV in comparison with patients without stroke (45.8 ± 21.0 vs 37.7 ± 16.9 ml; p < 0.05), and finite-diastolic volume of LV (114.3 ± 38.5 vs 100.9 ± 35.3 ml; p < 0.05), mainly in right hemispheric localization of stroke. Hypertrophy of ventricular septum (11.3 ± 2.1 mm) and the posterior wall of LV (10.4 ± 1.8 mm) was observed irrespective of localization of stroke, which was higher in comparison with patients without stroke (9.4 ± 1.5 mm). Violations of repolarization processes and their severity were characterized by higher values of duration of the corrected QT-interval in patients with structural changes of myocardium in comparison with patients without structural remodeling (0.46 ± 0.03 vs 0.44 ± 0.02 sec; p = 0.025). The conjugation of severity of neurological deficit (7+ points on NIHSS-scale) was associated with terminal-systolic size of LV (p = 0.025) and myocardial hypertrophy (11.3 ± 1.86 vs. 10.96 ± 1.8 mm; p = 0.04) in comparison with patients with neurological deficit < 7 points (31.7 ± 3.6 vs. 30.68 ± 3.86 mm; p < 0.025). The severity of neurological deficit according to Goldstein-criteria correlated with higher values of corrected (56.0 ± 23.93 vs 41.6 ± 23.3 ms; p = 0.043) and normalized QT (17.5 ± 6.53 vs 12.8 ± 6.7 ms; p = 0.019) values in comparison with lower neurological deficit. A similar relationship was revealed by Brott-criteria.

Conclusions:: Thus, direct connection between structural-electrical remodeling of heart and neurological deficit revealed in course of study reflects cardiocerebral relationships in IS.
ASSOCIATION BETWEEN IL1RN GENE POLYMORPHISMS AND POST-STROKE INFECTION

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Background and Aims:: Many genes may affect the outcome of stroke. Interleukin-1 receptor antagonist (IL-1ra) is an endogenous immunomodulatory cytokine encoded by IL1RN on chromosome 2. Elevated plasma IL-1ra is known to predict infection early after stroke, and polymorphisms in IL1RN may influence post-stroke infection risk. However, the role of IL1RN polymorphism on post-stroke infection is controversial. This study aimed to explore whether genetic polymorphism in IL1RN is associated with the risk of post-stroke infection in post-stroke dysphagia patients.

Methods:: A total of 218 subjects were enrolled in the study, and genotyping for IL1RN rs4251961 was carried out. Infection events (aspiration pneumonia, urinary tract infection, colitis, etc.) and the history of complications (admission to intensive care unit, history of intubation, septic shock, etc.) were recorded.

Results:: Data from 206 participants were available for final analysis. The baseline characteristics of patients with and without the minor C allele of the rs4251961 are shown on Table 1. There were no significant differences in age, sex, stroke type, diabetes, hypertension, atrial fibrillation, and coronary heart diseases between the patients with and without minor C allele. Post-stroke infection risk also did not show significant differences between two groups (Table 2).

<table>
<thead>
<tr>
<th>TT (n=177)</th>
<th>CT (n=27)</th>
<th>CC (n=2)</th>
<th>P-value</th>
<th>TT (n=177)</th>
<th>CT or CC (n=29)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>65.0 [55.0;73.0]</td>
<td>62.0 [57.5;75.5]</td>
<td>63.5 [53.0;74.0]</td>
<td>0.216</td>
<td>65.0 [55.0;73.0]</td>
<td>62.0 [56.0;74.0]</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>113 (63.8%)</td>
<td>21 (77.8%)</td>
<td>2 (100.0%)</td>
<td>0.216</td>
<td>113 (63.8%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>64 (36.2%)</td>
<td>6 (22.2%)</td>
<td>0 (0.0%)</td>
<td>0.216</td>
<td>64 (36.2%)</td>
</tr>
<tr>
<td>Stroke type</td>
<td>Infarct</td>
<td>99 (55.9%)</td>
<td>18 (66.7%)</td>
<td>2 (100.0%)</td>
<td>0.527</td>
<td>99 (55.9%)</td>
</tr>
<tr>
<td></td>
<td>Hemorrhagic</td>
<td>72 (40.7%)</td>
<td>9 (33.3%)</td>
<td>0 (0.0%)</td>
<td>0.527</td>
<td>72 (40.7%)</td>
</tr>
<tr>
<td></td>
<td>Combined</td>
<td>6 (3.4%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0.527</td>
<td>6 (3.4%)</td>
</tr>
<tr>
<td>DM</td>
<td>77 (43.5%)</td>
<td>7 (25.9%)</td>
<td>1 (50.0%)</td>
<td>0.218</td>
<td>77 (43.5%)</td>
<td>8 (27.6%)</td>
</tr>
<tr>
<td>HBP</td>
<td>132 (74.6%)</td>
<td>15 (55.6%)</td>
<td>2 (100.0%)</td>
<td>0.082</td>
<td>132 (74.6%)</td>
<td>17 (58.6%)</td>
</tr>
<tr>
<td>AFb</td>
<td>26 (14.7%)</td>
<td>6 (22.2%)</td>
<td>0 (0.0%)</td>
<td>0.5</td>
<td>26 (14.7%)</td>
<td>6 (20.7%)</td>
</tr>
<tr>
<td>CHD</td>
<td>23 (13.0%)</td>
<td>4 (14.8%)</td>
<td>0 (0.0%)</td>
<td>0.83</td>
<td>23 (13.0%)</td>
<td>4 (13.8%)</td>
</tr>
<tr>
<td>Recurrence of Stroke</td>
<td>33 (18.6%)</td>
<td>8 (29.6%)</td>
<td>0 (0.0%)</td>
<td>0.321</td>
<td>33 (18.6%)</td>
<td>8 (27.6%)</td>
</tr>
<tr>
<td>CHD + Recurrence of Stroke</td>
<td>51 (28.8%)</td>
<td>11 (40.7%)</td>
<td>0 (0.0%)</td>
<td>0.293</td>
<td>51 (28.8%)</td>
<td>11 (37.9%)</td>
</tr>
</tbody>
</table>
Conclusions:: Genetic polymorphism of IL-1RN failed to effectively reflect the post-stroke infection risk in post-stroke dysphagia patients. The risk of post-stroke infection may be affected by multifactorial reasons. Further long-term studies and studies of other genetic polymorphisms on infection are warranted. *This work was supported by the National Research Foundation of Korea(NRF) grant funded by the Korea government(MSIT) 2017R1C1B5017926.
ANTERIOR CIRCULATION LARGE VESSEL OCCLUSION STROKE IN SAUDI ARABIA: PREVALENCE, PREDICTORS, AND OUTCOME

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Background and Aims:: Anterior circulation Large Vessel Occlusion (LVO) stroke comes with significant morbidity and mortality. With the advent of endovascular interventions, its management has revolutionized. For health authorities to build systems and allocate resources, its burden, predictors, and outcome must be determined.

Methods:: We retrospectively collected data from 1,495 ischemic stroke patients in a single tertiary care center to determine anterior circulation LVO prevalence, predictors, and outcome. Patients must have radiologically proven ischemic stroke within 24 hours before arrival at the emergency department. An anterior circulation LVO stroke was defined as a new anterior circulation infarct detected on neuroimaging/vascular imaging confirming anterior circulation LVO. Data on demographics, vascular risk factors, treatment with reperfusion therapy, modified Rankin Scale (mRS) at admission, National Institute of Health Stroke Scale (NIHSS) at admission, length of stay (LOS) in days, and in-hospital comorbidities and death were collected.

Results:: We found anterior circulation LVO in 27.8% of all ischemic stroke patients. Atrial fibrillation and NIHSS at admission were the strongest predictors of LVO [OR 2.33, P = 0.0011 and OR 1.17, P < 0.0001] respectively. Occurrence of LVO was associated with worse disability score (mRS ≥ 3) [47.22 vs. 19.81% (P = 0.0073)], longer hospitalization in days [Median 9.0 vs. 3.0, P = 0.0432)], and was more likely to result in patient admission to the ICU [Mean 17.59 vs. 3.70 % (P = 0.0002)].

Conclusions:: Stroke with large vessel occlusion in Saudi Arabia is not uncommon. Its burden and outcome deserve national attention, as effective treatment is now readily available.
STROKE MIMICS: CLINICAL CHARACTERISTICS AND OUTCOME

Mohammed Aldriweesh¹, Ali Al Khathaami², Sultan Alsaif³, Bayan Albdah⁴, Muath Alhasson⁵, Wangde Alužidane⁶, Faisāl Almutairi¹, Jawaher Alotaibi⁷, Mohammed Alsaini²
¹King Saud bin Abdulaziz University for Health Sciences, College Of Medicine, Riyadh, Saudi Arabia, ²King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Division Of Neurology, Department Of Medicine, Riyadh, Saudi Arabia, ³Almaarefa College, College Of Medicine, Riyadh, Saudi Arabia, ⁴King Abdullah International Medical Research Center, Department Of Biostatistics And Bioinformatics, Riyadh, Saudi Arabia, ⁵Qassim University, Unaizah College Of Medicine, Unayzah, Saudi Arabia, ⁶Imam Muhammad bin Saud Islamic University, College Of Medicine, Riyadh, Saudi Arabia, ⁷Princess Nourah Bint Abdul Rahman University, College Of Medicine, Riyadh, Saudi Arabia

Background and Aims:: Stroke mimics (SM) are often misdiagnosed as real stroke among patients who came to the emergency department with a sudden neurological deficit and negative neuroimaging. We aimed to study the prevalence and nature of stroke mimics among suspected stroke patients.

Methods:: We retrospectively reviewed all electronic health records of patients suspected of having a stroke in a single tertiary center. Also, we established a comparison between SM and stroke. Our study identified the predictors of SM by using logistic regression analysis.

Results:: Out of 1,063 patients, 131 (12.3%) had SM. The most common causes were peripheral vestibular disorder (27.4%), followed by psychogenic causes (24.4%). Stroke mimics were more common among younger individuals and women. Arterial hypertension, diabetes, and smoking were less likely to be found in SMs. At discharge, individuals with SM were more likely to be independent, had milder deficits, and shorter hospital stays. Predictors of SM were young age, female gender, mild deficit at presentation, and good functional status before the stroke.

Conclusions:: The incidence of stroke mimics is common among suspected stroke patients. Practicing physicians should consider potential diagnostic errors, especially in the hyperacute phase of the stroke. Stroke mimics should be suspected at a young age, mild deficit at presentation, and good functional status before the acute neurological deficit.
ASSOCIATION OF POSTERIOR DIVISION MCA STROKE LOCATION WITH POPULATIONAL INCIDENCE OF ATRIAL FIBRILLATION

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Background and Aims:: Anatomical features of Middle Cerebral Artery (MCA) bifurcation favors larger emboli entering the posterior rather than anterior division[1]. As cardiac source emboli are on average larger than arterial source emboli, we hypothesize that groups with higher incidence of atrial fibrillation, a major cause of cardioembolic strokes, have more strokes in temporal and parietal lobes compared to frontal lobes. [1] Liebeskind DS, et al. Stroke.2000;31:294.

Methods:: From 1,878 patients admitted to the Johns Hopkins Stroke Center (2009- 2019) with evidence of acute or early subacute ischemic stroke (2-24h post-onset) on diffusion-weighted MRI (DWI), 482 affected exclusively the “lobar” MCA (sparing the lenticulostriates). They were classified as “frontal predominant” (n=106) if ≥75% of the stroke was in the frontal lobe, or “temporoparietal predominant” (n=220), by the same criterion. Two evaluators and a neuroradiologist defined the stroke in DWI. Differences between stroke location (frontal or temporoparietal), sex, and race-ethnicity were analyzed by Chi-square test.

Results:: The groups (frontal or temporoparietal strokes) were balanced in age and sex. Men were more likely than women to have temporoparietal strokes (74% vs 61%) versus frontal strokes (p=0.01). Similarly, white patients were more likely than black patients to have temporoparietal strokes (73% vs 58%) versus frontal strokes (p=0.01).

ULTRASOUND-GUIDED DIAGNOSIS OF AN UNCOMMON STROKE: A CASE OF GIANT CELL ARTERITIS

Sara Giannoni¹, Mariella Baldini¹, Elisa Cioffi², Elisa Grifoni², Elisabetta Bertini¹, Eleonora Cosentino², Cinzia Grisanti¹, Serena Colon¹, Leonello Guidi¹, Luca Masotti²
¹San Giuseppe Hospital, Department Of Neurology, Empoli, Italy, ²San Giuseppe Hospital, Internal Medicine, Empoli, Italy

Background and Aims:: Giant cell arteritis (GCA) is an immune-mediated vasculitis of large- and medium-sized vessels like superficial temporal arteries, extradural vertebral (VA) and carotid arteries (CA). Stroke happens in 3% to 7% of the cases and identifying GCA properly is important because potentially curative treatment exists.

Methods:: An 83-year-old woman had a sudden onset of postural instability and bilateral hypoacusia. Laboratory tests didn’t show significant pathological findings. TC-Angiography showed a filiform lumen of right VA and occlusion of V3-V4 segment of left VA, right AICA and left PICA. Brain MRI pointed out restricted diffusion lesions in bilateral cerebellar dentate nuclei, consistent with acute ischemic stroke (Figure 1).

Ultrasonography didn’t show relevant anomalies in CA; instead, VA presented an homogeneous, hypoechogenic and concentric dark area (the so-called “halo sign”) around the lumen of the bilateral V2 segment (Figure 2).
The uncommon stroke localization and the ultrasound findings suggested vasculitic etiology of lesions, like GCA. So an ultrasound examination of the TA was performed and, interestingly, it highlighted the “halo sign” also in the bilateral temporal arteries. MR-angiography confirmed the previous intracranial vascular findings. Finally, the patient performed a 18FDG-PET which highlighted increased FDG uptake of inflamed vertebral artery walls.

**Results:** Patient was treated with a high dose of iv steroids and oral antiplatelet therapy, with improvement of clinical status.

**Conclusions:** In our patient clinical diagnosis of GCA was challenging due to limited classical symptoms. Arguments in favor of arteritis were the symmetric involvement of the VA, the sonographic halo sign and atypical stroke localization.
PROSPECTIVE PILOT STUDY TO ASSESS MOTOR ACTIVITY AND THE STATE OF THE HEMOSTASIS SYSTEM IN THE ACUTE PERIOD OF ISCHEMIC STROKE DURING SYSTEMIC THROMBOLYTIC THERAPY

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UMSA, Neurology, Kremenchug, Ukraine

Background and Aims:: To investigate changes in motor activity and indicators of the state of the hemostasis system in the acute period of ischemic stroke during systemic thrombolytic therapy (sTLT) and without its use.

Methods:: We examined 26 male and female patients with a clinical diagnosis of ischemic stroke, who were hospitalized on the first day of the disease to the neurological departments. Patients were divided into 2 groups: group 1 - patients who underwent sTLT (n = 11), group 2 - patients who did not receive sTLT (n = 15). To compare the coagulogram parameters, 12 healthy patients were examined (control group). Examination of patients was performed on the 1st and 14th day of the disease (clinical examination, assessment of motor activity, coagulation test). Stroke severity was determined by the overall score of the National Institutes of Health Stroke Scale.

Results:: The average age of patients in group 1 - 60.1 ± 8.2 years old, in group 2 - 61.3 ± 5.5 years old. The number of points on the NIHSS scale in group 1 was 8.8 ± 1.13 on the 1st day and 3.7 ± 0.79 on the 14th day (p < 0.05), in group 2 - 5.7 ± 0.94 on the 1st day and 3.1 ± 0.93 on the 14th day (p < 0.05). The results of the study of the coagulogram indicate a significantly higher level of soluble fibrin-monomer complexes on the 1st day on the 14th day of the ischemic stroke.

Conclusions:: In the acute period of ischemic stroke changes in the hemostasis system reflected the direction of the selected therapy. The use of systematic thrombolytic therapy in ischemic stroke led to a more severe decrease in stroke severity on the NIHSS scale, a significant increase in Barthel index.
Background and Aims:: Babinski-Nageotte Syndrome (BNS) is one of the brainstem syndromes presenting with classic Wallenberg findings with associated contralateral motor deficit. Based on our literature review, only few cases have been reported and none of them was due to aneurysmal compression of the medulla oblongata. This paper aims to present a case of a 42-year old Filipino male, married, construction worker who manifested with sudden onset of severe headache with associated vertiginous dizziness, dysphagia, dysphonia, nausea, vomiting, and right extremity numbness and hemiparesis.

Methods:: Magnetic Resonance imaging (MRI) was done revealing no evidence of acute territorial infarct or hemorrhage, and Cranial CT Angiography and Digital Subtraction Angiography showed an unruptured fusiform aneurysm of the left vertebral artery (VA) involving the proximal intracranial segment.

Results:: The clinical and radiologic evidence were consistent with a left vertebral fusiform aneurysm compressing on the medulla and clinically manifesting as Babinski-Nageotte Syndrome.

Conclusions:: Diseases of the vertebral arteries result to neurologic symptoms through different mechanisms. Direct medullary compression should be highly considered for certain patients manifesting with symptoms that are gradual and persistent. It is important to have a high index of suspicion for the presence of certain arteriopathies such as aneurysm as it can be a potential mechanism for ischemic injury by generating pressure on perforating branches. This case of Babinski-Nageotte Syndrome resulting from medullary compression from a vertebral artery aneurysm may pave way to better understand this rare disease and its corresponding treatment approach based on the mechanism of disease evolution.
COGNITIVE IMPAIRMENTS AND VASCULAR ENDOTHELIAL DYSFUNCTION IN UNILATERAL OCCLUSION OF THE CAROTID ARTERY

Sergey M. Gulyaev
Institute of General and Experimental Biology, Siberian Branch of the Russian Academy of Sciences, Laboratory Of Experimental Pharmacology, Ulan-Ude, Russian Federation

Background and Aims:: The study was aimed at determining cognitive impairments, vascular endothelial dysfunction and alterations of neurons in brain structures in unilateral occlusion of the common carotid artery.

Methods:: The experiments were carried out on Wistar rats. The animals were divided into two groups: 1 – the control group composed of sham-operated rats, 2 – rats with cerebral ischaemia. The model of cerebral ischaemia was reproduced by occlusion of the left common carotid artery. Cognitive functions in rats were assessed by means of the object recognition test and conditioned passive avoidance response. The degree of vascular endothelial dysfunction was evaluated by the number of circulating endotheliocytes and concentration of nitric oxide in plasma. Morphological studies of the brain were carried out by means of light microscopy.

Results:: It was determined that unilateral occlusion of the carotid artery in rats resulted in memory impairment revealed by cognitive tests. Cerebral ischaemia induced an elevated level of circulating endotheliocytes and a decrease of nitric oxide (p≤0.05). Morphological study demonstrated signs of vasoconstrictive reactions, microvascular endothelial oedema, as well as an increase number of damaged neurons localized in the neocortex and hippocampus on the ipsilateral side as compared with the controls (p≤0.05).

Conclusions:: Unilateral occlusion of the common carotid artery in rats resulted in cognitive impairments, damage of neurons in the neocortex and hippocampus predominantly on the ipsilateral side. Cognitive impairments and ischaemic lesions of the brain are induced by endothelial dysfunction, enhanced desquamation of endotheliocytes and prevalence of vasoconstrictive reactions resulting from decreased production of the nitric oxide.

This research was funded by the Ministry of Education and Science of Russia, grant number - 121030100227-7
HEMORHEOLOGICAL EFFECT OF HERBAL EXTRACT IN CEREBRAL ISCHEMIA-REPERFUSION

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Laboratory Of Experimental Pharmacology, Ulan-Ude, Russian Federation

Background and Aims:: The aim of this study was to determine hemorheological and neuronal disorders in cerebral ischemia-reperfusion and to assess the neuroprotective effect of a complex herbal extract (Astragalus membranaceus, Scutellaria baicalensis, Phlojodicarpus sibiricus).

Methods:: Male Wistar rats were divided into three groups: sham group; ischemia-reperfusion group and herbal extract group. Cerebral ischemia-reperfusion model was induced by occlusion of common carotid arteries for 5 min followed by reperfusion for 72 h. We investigated the effect of herbal extract at a dose of 100 mg/kg on erythrocyte deformability, blood viscosity, and hemostasis parameters. After experiments, rats were euthanized and the brain was taken for histological analysis.

Results:: In rats with cerebral ischemia-reperfusion, as compared to sham, erythrocytes and trombocytes aggregation, blood viscosity were increased and erythrocyte deformability were decreased, (p<0.05). These hemorheological alterations were present in duaring 72 hrs. In rats with cerebral ischemia-reperfusion, herbal extract improved all of the above parameters (p<0.05). Cerebral ischemia-reperfusion in rats (no treated) caused injuries in the brain. The herbal extract exerted a neuroprotective effect.

Conclusions:: The results show that even short-term ischemia-reperfusion of the brain leads to hemorheological and neuronal disorders, which can be largely corrected by herbal extract. The data obtained indicate that the herbal extract has a neuroprotective effect by regulating hemorheological parameters. Thus, extract is a promising stroke prevention agent.

This research was funded by the Ministry of Education and Science of Russia, grant number - 121030100227-7.
NOTCH3 NEGATIVE CADASIL: A CASE REPORT

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¹Worcester Royal Hospital, Stroke Unit, KEIGHLEY, BRADFORD, United Kingdom, ²Worcester Royal Hospital, Stroke Unit, Worcester, United Kingdom, ³Worcestershire Acute Hospital NHS Trust, Stroke Medicine, Worcester, United Kingdom

Background and Aims:: CADASIL is a rare disease diagnosed mainly after genetic testing of NOTCH3 mutation on chromosome 19. >170 mutations have been found till now. However, it can still be diagnosed in patients who have no NOTCH3 mutation provided they have characteristic signs and symptoms with recurrent strokes, migraine, cognitive deficits, and neuropsychiatric issues complemented by typical MRI brain findings and suggestive family history.

Methods:: 50 year old male presented with classic migraine, recurrent TIAs and strokes, rapidly progressive decline in memory and executive function since age of 37 years. He had diabetes, hypertension, asthma, anxiety and depression. His father had stroke at age<60 and cousin of similar age had migraine, cognitive decline and recurrent strokes. His son in his 20s had migraine and psychiatric problems. MRI showed lacunar infarcts bilaterally involving basal ganglia, internal capsule, thalamus, pons, and subcortical areas in frontal, parietal and occipital lobes and multifocal micro-haemorrhages. Extensive stroke in young workup including MRA head and neck, ECHO, thrombophilia and vasculitis screen was unremarkable. However, NOTCH3 gene mutation test was negative.

Results:: He was discussed in MDT with neurologist, and neuroradiologist. It was decided he should be treated as NOTCH3 negative CADASIL. Referral was done to higher centre for second opinion and they agreed with our diagnosis.

Conclusions:: Some features are more frequent in CADASIL than NOTCH3 negative cases; however, these are not pathognomonic. CADASIL can be diagnosed clinically in absence of gene mutation. Further research is needed to find out NOTCH3 variants gene mutations that may be responsible in these patients.
IN HOSPITAL MORTALITY AND SHORT-TERM OUTCOME OF ACUTE ISCHEMIC STROKE PATIENTS CONTRACTING SARS COV-2 INFECTION: EXPERIENCE FROM A DEDICATED STROKE UNIT IN BANGLADESH

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Background and Aims:: In this study we intended to evaluate the influence of COVID-19 on in hospital mortality and short-term outcome of acute ischemic stroke.

Methods:: This was a hospital-based case-control study from February to May 2021 conducted in stroke unit of National Institute of Neurosciences and Hospital. Fifty consecutive ischemic stroke patients contracting COVID-19 infection was considered as cases (group-B) and 99 similar patients, negative for SARS CoV-2 on RT-PCR from nasal swab were considered for control group (group-A) following the inclusion and exclusion criteria.

Results:: Diabetes and Multiple comorbid conditions and lymphopenia were significantly (p value of <0.001) more common in Group B (1% versus 22%, 28.3% versus 56% and 5.1% versus 54%) in contrast to Hypertension and lymphocytosis which was more frequent in Group A (42.4% versus 10% and 94.9% versus 46%). The patients in group B had a significantly (p value <0.001) higher NIHSS score at admission (median IQR 7 versus 13) and longer hospital stay (median IQR 6 days versus 14 days). There was no significant difference among the groups in mRS at discharge (median IQR 3) and at 30 days with a median IQR of 2. Male stroke patients are 4.7 times more likely to die in-hospital. The risk of mortality is 5 times higher among COVID positive stroke cases.

Conclusions:: Diabetes, Multiple comorbid conditions and lymphopenia are common association in COVID positive stroke cases. The risk of mortality is 5 times higher in COVID positive stroke cases and 4.7 times among the male.
Background and Aims:: Stroke is a global public health problem. In general, there are 2 types of stroke, ischemic accounting for 80% and hemorrhagic 20% of all strokes. Currently, the opposite of this epidemiological profile is observed in the Neurology Training and Research Unit (USFR) at the Befelatanana University Hospital Center (HUC).

Methods:: We have a descriptive retrospective study conducted at the USFR neurology, CHU Befelatanana from January 1, 2017 to December 31, 2017. We have included all records whose exit diagnosis is a stroke made up with clinical and radiological confirmation.

Results:: We selected 201 male-dominated patients, 55% of whom were hemorrhagic and 45% ischemic. The average age of 51.01 for hemorrhagic stroke and 58.58 years in ischemic stroke. Growers are most affected 26.37% (n=24) in ischemic stroke and 35.45% (n=39) of hemorrhagic strokes. The majority of patients live in urban and married settings. Ischemic stroke is predominantly of cardiac origin in 32.86% (n-29) while high blood pressure (HTA) is responsible for hemorrhagic strokes in 66.36% (n -73). The average National Institute of Health Stroke Score (NIHSS) is 15.17 in cerebral ischemia and 18.32 in cerebral hemorrhage. We have 43 deaths of which 17 (17.45%) hemorrhagic fever and 26 (28.57%) ischemic. Survivors after ischemic stroke have a Rankin score ≥ 3 and 45.16% (n=42) of hemorrhagic stroke have a severe disability with Rankin score ≥ 4.

Conclusions:: The prevalence of hemorrhagic stroke associated with high blood pressure is the main feature of this pathology at the Befelatanana University Hospital.
ASSOCIATION OF ELEVATED BODY MASS INDEX WITH MORTALITY FOLLOWING ACUTE ISCHEMIC STROKE: THE OBESITY PARADOX REVISITED

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Background and Aims:: Previous literature has identified a survival advantage in acute ischemic stroke (AIS) patients with elevated body mass indices, a phenomenon termed the “obesity paradox”.

Methods:: Weighted discharge data from the National Inpatient Sample were queried to identify AIS patients from 2015-2018. Multivariable logistic regression and Cox proportional hazards modelling were performed to evaluate adjusted and time-dependent associations between obesity (BMI ≥ 30) and clinical endpoints after controlling for acute stroke severity and comorbidity burden.

Results:: Among 1,687,805 AIS patients, 216,775 (12.8%) were obese. Compared to non-obese individuals, these patients were younger (64 vs. 72 mean years), had lower baseline NIHSS scores (6.9 vs. 7.9 mean score), and a higher comorbidity burden. Multivariable analysis demonstrated independent associations between obesity and lower likelihood of mortality (adjusted odds ratio (aOR) 0.76, 95% CI 0.71, 0.82, p<0.001; hazard ratio (HR) 0.84, 95% CI 0.73, 0.97, p=0.015), intracranial hemorrhage (aOR 0.87, 95% CI 0.82, 0.93, p<0.001), and routine discharge to home (aOR 0.97, 95% CI 0.95, 0.99; p=0.015). Sensitivity testing to account for baseline NIHSS score extended confirmed these findings. Mortality rates between obese and non-obese patients were significantly lower across stroke severity thresholds, but this difference was attenuated among high severity (NIHSS>20) strokes (21.6% vs. 23.2%, p=0.358).

Conclusions:: This population-based, cross-sectional analysis demonstrates a lower likelihood of discharge to home as well as in-hospital mortality following AIS, suggestive of a protective effect of obesity against mortality but not against all post-stroke neurological deficits in the short term. This effect may be attenuated among strokes of high severity.
Background and Aims:: ABSTRACT
BACKGROUND: The incidence of Ischemic Stroke among young adult (16-50 years) is rising and is currently estimated to constitute up to 15% of all Ischemic Stroke, the prevalence of modifiable vascular risk factors for Stroke, such as Dyslipidemia, Smoking and Hypertension are highly prevalent in young population.
Methods:: this is a prospective Analytical Study
Results:: Clinical presentation was varying from Hemiparesis 62(98.6%), Hemiplegia 18(33.75%), Dysphasia 39(48.75%), Aphasia 23(28.75%), hemisensory loss 27(33.75%), Headache 7(8.75%), Visual disturbance 7(8.75%), Dysarthria 5(6.25%), seizures 5(6.25%), Disturbed level of Consciousness 4(5%) and Sphincteric disturbance 3(3.8%).
Conclusions:: CONCLUSION: Ischemic Stroke is common among young adult males Sudanese patients, Modifiable risk factors, such as Hypertension, Diabetes Mellitus, Dyslipidemia, Smoking and Obesity were increasing due to change of life style, Diet and lack of Exercise.
Background and Aims:: This study was conducted to clarify the risk factors of unfavorable early outcomes (UEO) in acute mild ischemic stroke (AMIS).

Methods:: Patients with AMIS, defined as a National Institute of Health Stroke Score (NIHSS) < 4 and admission within 48 hours after symptoms onset, were prospectively registered. A favorable outcome was defined as a modified Rankin Scale (mRS) of 1 or lower. Risk factors of UEO were analyzed.

Results:: From Sep 01, 2015 to April 30, 2020, 629 patients with AMIS were included. At discharge, 144 patients had UEO (22.9%). Patients with UEO were older (68.1 ± 13.2 vs 63.0 ± 13.4 years, p=0.000) and with higher prevalence of hypertension (85.4 vs 76.1%, p= 0.016), and higher initial NIHSS (2.1 ± 1.0 vs 1.1 ± 1.1, p=0.000). Blood tests showed lower platelets count (217.0 ± 75.5 vs 235.4 ± 85.0 k/cumm, p=0.005), higher casual plasma glucose (151.2 ± 74.5 vs 139.3 ± 67.8 mg/dl, p= 0.007), and higher high-sensitivity C-reactive protein (0.8 ± 2.0 vs 0.5 ± 1.4 mg/l, p=0.037) in patients with UEO. In addition, patients with UEO were less likely to have dual antiplatelets (aspirin and clopidogrel) at discharge. Multivariate analysis demonstrates that higher initial NIHSS (odd ratio, 2.12, 95% CI, 1.60-2.80, p=0.000) and no dual antiplatelets at discharge (odd ratio, 1.83, 95% CI, 1.01-3.31, p=0.046) are independent risk factors for UEO.

Conclusions:: Higher initial NIHSS score and no dual antiplatelets at discharge are independent risk factors for unfavorable early outcomes.
RECOVERY TO BE REPLACED WITH ARM USE.

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Background and Aims:: About 82% of the needs expressed by stroke survivors indicated that they had a substantial need for information and struggle with understanding their condition and treatment options. Studies show that patient knowledge deficits can be a barrier to exercise adherence, which is vital for improved health outcomes and functional independence. There is a need for identifying various knowledge domains and applying strategies to specifically target them to improve exercise adherence in stroke survivors. The aim of the study is to determine the extent to which experts in the field of Neuro Physiotherapy agree with various domains of knowledge deficit in stroke survivors pertaining arm dysfunction, intervention, contextual limitations and recovery options.

Methods:: We first conducted a literature review to identify knowledge constructs needed for promoting a behavior. We ran rounds of Delphi with 8 expert neurological physiotherapists involved in stroke rehabilitation. They identified domains of knowledge relevant to promoting affected arm use after stroke. Consensus was reached after 3 rounds of Delphi.

Results:: 4 knowledge constructs based on Theoretical domains framework were knowledge of effect of lack of arm use; rationale for arm use; procedural knowledge and facilitatory contexts for promoting arm use. Experts identified various subdomains in each of these domains.

Conclusions:: The subdomains identified can be used for educating stroke survivors to promote optimal affected arm use for recovery.
IMPACT OF DELIRIUM PERSISTENCE ON STROKE OUTCOMES

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UFBA, Neurology, Salvador, Brazil

Background and Aims:: Delirium is a condition that usually resolves itself, but recent studies have shown its negative impact on long term prognosis. This phenomenon is not well studied in medical literacy, so we aim to evaluate the influence of delirium persistence on stroke outcomes.

Methods:: Prospective cohort of stroke patients with symptom onset within 72 hours of admission who developed delirium during hospitalization. Delirium was assessed daily by the Confusion Assessment Method in an Intensive Care Unit (CAM-ICU). When a patient had no delirium for 48h after a positive CAM-ICU, the delirium was considered to be resolved. However, when there was another positive delirium screening in this period, delirium was classified as persistent. We assessed a composite outcome of functional dependence (measured by Modified Rankin Scale > 2) and mortality in 90 days.

Results:: Out of 121 delirium patients, 95 were followed until discharge. Our sample’s mean age was 65.8 (± 15.7) years and the frequency of persistent delirium was 67.4%. Delirium persistence was associated with increased risk of death and functional dependence in 90 days compared to non persistence (84.4% versus 42.9%; Chi²=15.9; p<0.001). Multivariate analysis showed delirium persistence as independent predictor of worse outcome (OR=5.8 [95% CI, 1.7–20.2]; p<0.01), besides NIHSS on admission.

Conclusions:: Among stroke delirium patients, the persistence of this condition during hospitalization is frequent. This phenomenon seems to predict worse outcomes in this population. From what we gather, it's the first study to prospectively investigate the impact of delirium duration over functional outcome and mortality three months poststroke.
ELECTROCARDIOGRAPHIC CHANGES AND SERUM TROPONIN LEVELS IN PATIENTS WITH ACUTE STROKE, A PROSPECTIVE COHORT STUDY IN SUDAN

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Background and Aims:: Electrocardiographic changes and elevated serum troponin are frequent findings in acute stroke. They may reflect what is known as the neuro-genic myocardial injury. However, as stroke and cardiac disease share the same risk factors, Coexistence of the two is highly susceptible. Our aim to determine the electrocardiographic changes and serum troponin level in acute stroke patients and to correlate these changes to the anatomical location and pathological type of the stroke.

Methods:: A Prospective cohort study conducted at the national center of neurological Science, from January to December 2019. Study was done at the neurological center in Sudan, The National Center of Neurological sciences. All cases presented with acute stroke during the study period were included. Non-probability sample, with total coverage during study period. 50 patients were included in the study. Data were analyzed by using (SPSS) version 25. 12 standard ECG were performed in the first hours of admission. 2 samples from each patient were obtained for serum troponin with at least 8 hours apart.

Results:: All patients had wide variants of ECG changes. But tachycardia was the most frequent one identified in 54% of patients (27/50). Half of them were found to have an anterior circulation stroke. 14% of patients (7/50) have positive troponin, ECG changes identified in all of patients who represent positive troponin 100% (7 patients). Moreover, anterior circulation stroke was recognized in all patients with positive troponin I marker.

Conclusions:: This study suggest that ECG abnormalities in patients with acute stroke are very common, especially tachycardia. The site of lesion appear to play major factor as a cause of genesis of arrhythmia. Concomitant cardiac diseases may present. Serum troponin elevation may play a role in diagnosing neuro-cardiogenic injury but, ECG appears to be more sensitive and familial.
IS THROMBOCYTOPENIA A RISK FACTOR OF IN-HOSPITAL MORTALITY AMONG PATIENTS WITH CEREBRAL INFARCTION WITHOUT ACUTE REPERFUSION THERAPY: A PROPENSITY SCORE-MATCHED ANALYSIS FROM THE MIMIC-IV DATABASE

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Background and Aims:: The aim of study is to investigate the clinical characteristics and outcomes of patients with cerebral infarction and thrombocypenia (TP) without reperfusion therapy in intensive care units.

Methods:: In the Medical Information Mart for Intensive Care IV database, patients with cerebral infarction were enrolled from 2008 to 2019 (Figure 1). TP was defined as <150 × 10⁹/L. The clinical characteristics of patients with and without TP were compared using propensity score matching (PSM). Propensity scores were estimated using the following covariates: age, sex, Charlson Comorbidity Index (CCI), Acute Physiology Score (APS) III, and HAS-BLED score. A Cox proportional hazards model was used to determine the nonlinear association between TP and in-hospital mortality in patients with cerebral infarction.
Results: Of the 1,070 patients, 141 patients (13.2%) had TP. Patients with TP were older (71.0±12.9 v.s. 68.4±14.5; P=0.048) and had higher CCI (7.3±2.5 v.s. 6.8±2.7; P=0.063), APS III (39.4±19.2 v.s. 34.3±15.9; P=0.001), HAS-BLED score (3.9±1.0 v.s. 3.7±0.9; P=0.021), and in-hospital mortality (26/141, 18.4% v.s. 112/929, 12.1%; P=0.035) than those without TP (Table 1). Platelet count did not associate with in-hospital mortality (Figure 2). After 1:4 PSM, 647 patients remained (TP group: 137, non-TP group: 510; respectively). The cohorts were well-balanced based on five covariates between the TP and non-TP groups. TP was not associated with higher in-hospital mortality (HR: 1.18, 95% CI: 0.74–1.87).
Table 1. Characteristics of the study patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All patients</th>
<th>Propensity-matched pairs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TP group</td>
<td>Non-TP group</td>
</tr>
<tr>
<td></td>
<td>(n = 141)</td>
<td>(n = 929)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>71.00±12.90</td>
<td>68.44±14.51</td>
</tr>
<tr>
<td>Gender (Female), n</td>
<td>43(30.3%)</td>
<td>471(50.7%)</td>
</tr>
<tr>
<td>Comorbidities, n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCI</td>
<td>7.27±2.46</td>
<td>6.83±2.65</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without chronic complication</td>
<td>31(22.0%)</td>
<td>264(28.4%)</td>
</tr>
<tr>
<td>With chronic complication</td>
<td>11(7.8%)</td>
<td>79(8.5%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>19(13.5%)</td>
<td>123(13.2%)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>27(19.1%)</td>
<td>181(19.5%)</td>
</tr>
<tr>
<td>PVD</td>
<td>18(12.8%)</td>
<td>102(11.0%)</td>
</tr>
<tr>
<td>COPD</td>
<td>20(14.2%)</td>
<td>170(18.3%)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>33(23.4%)</td>
<td>125(13.5%)</td>
</tr>
<tr>
<td>HAS-BLED score</td>
<td>3.87±0.99</td>
<td>3.68±0.92</td>
</tr>
<tr>
<td>APS III</td>
<td>39.38±19.20</td>
<td>34.27±15.85</td>
</tr>
<tr>
<td>ICU mortality, n</td>
<td>16(11.3%)</td>
<td>64(6.9%)</td>
</tr>
<tr>
<td>ICU length of stay, day</td>
<td>5.23±6.98</td>
<td>4.44±5.87</td>
</tr>
<tr>
<td>In-hospital mortality, n</td>
<td>26(18.4%)</td>
<td>112(12.1%)</td>
</tr>
<tr>
<td>Hospital length of stay, day</td>
<td>9.06±9.70</td>
<td>7.96±8.89</td>
</tr>
<tr>
<td>Intracranial hemorrhage, n</td>
<td>17(12.1%)</td>
<td>99(10.7%)</td>
</tr>
</tbody>
</table>

Propensity score matching by age, sex, Charlson comorbidity Index, acute physiology score III, and HAS-BLED score.
APS III: acute physiology score III; BUN: blood urea nitrogen; CCI: Charlson comorbidity Index; COPD: chronic obstructive pulmonary disease; Hgb: hemoglobin; PVD: Peripheral vascular disease; WBC: white blood cell.
#: Testing by Fisher exact test or Wilcoxon Test, respectively.
Conclusions: Thrombocytopenia could be associated with poor clinical characteristics and in-hospital mortality; however, it is not an independent short-term risk factor of in-hospital mortality among patients with cerebral infraction without reperfusion therapy.
SOCIO-DEMOGRAPHIC FACTORS AND RISK FACTORS RELATED TO ISCHEMIC STROKE SUBTYPES AND OUTCOMES IN A TERTIARY CARE HOSPITAL IN SRI LANKA.

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Background and Aims:: Stroke is a heterogeneous, catastrophic disease. An in-depth clinical analysis of ischemic stroke(IS) risk factors and outcome is crucial for optimum management in resource-poor settings. The current study aimed to describe the acute-cerebrovascular-disease(ACVD) subtypes and subtype-categories with risk factors, severity, and outcomes.

Methods:: A prospective cross-sectional study of ACVD patients was conducted in a tertiary care center in Sri Lanka. Risk factors, severity, and outcomes of individual IS subtype and subtype-categories were studied based on the Oxfordshire-Community-Stroke-Project-Clinical classification.

Results:: Among 592 patients involved, IS was the commonest(63.3%). Partial anterior circulation syndromes(PACS) total anterior circulation syndrome(TACS), posterior circulation syndromes(POCS) and lacunar syndromes(LACS) accounted for 102(29.7%),58(16.9%), 88(25.7%) and 95(27.7%) respectively. Commonest PACS sub-category was higher-cerebral-dysfunction-with-homonymous-hemianopia(HCD+HH)(39;38.2%). Cerebellar-signs-without-long-tract-signs(CS-LTS) sub-category constituted the highest among POCS(47;53.4%). The commonest sub-category within LACS was pure-motor(PM) strokes(43;45.3%). Patients with age≥50 years(Adjusted-OR,2.439; 95%CI,1.163-5.116;P-0.018), ischemic-heart-disease(Adjusted-OR,2.520; 95%CI,1.347-4.713;P-0.004) and body-mass-index >23kg/m²(Adjusted-OR,2.607; 95% CI,1.420-4.784; P-0.002) were at 2.5 fold risk of TACS. Patients with a history of transient-ischaemic-attack(adjusted-OR,1.910; 95%CI,1.036-3.524; P-0.038) and arrhythmias(adjusted-OR,5.933; 95%CI,3.294-10.684; P<0.001) were at 1.9 and 5.9 fold higher risk for POCS respectively. A patient with hypertension was 2.3 times at risk of LACS(adjusted-OR,2.233; 95%CI,1.270-3.926; P-0.005). NIHSS(<P<0.001), mRS on admission(<P-0.001) and in 3 months(<P<0.001), deaths during hospital stay(<P-0.001) and within 28 days(<P<0.001) had a statistically significant relationship with individual stroke subtypes

Conclusions:: The comparative risk of different IS subtypes vary based on different risk factors. The findings of this study signify that sub-categories within each stroke subtypes may behave independently with regards to risk factors and outcomes, thus warranting the need for individual assessment.
MODIFIED 8DS ALGORITHM IMPROVES DOOR-TO-NEEDLE TIME IN PATIENTS WITH ACUTE ISCHEMIC STROKE ELIGIBLE FOR ALTEPLASE OR THROMBECTOMY; A PROSPECTIVE COHORT STUDY.

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Background and Aims:: Timely restoration of cerebral blood flow using reperfusion therapy (RT) is the most effective strategy for salvaging ischemic brain tissue that is not already dead. There is a narrow window for RT since its benefit decreases over time. Intravenous thrombolysis (IVT) and mechanical thrombectomy (MTE) are key elements of acute ischemic stroke (AIS) management resulting in more favorable outcomes. Herein, we aimed to monitor risk factors, management, and outcome of patients with AIS eligible for IVT/MTE.

Methods:: In this ongoing prospective cohort study, we enroll AIS patients eligible for IVT/MTE who are referred to our Comprehensive Stroke Center within 4.5 or 6h of presenting symptoms between September 2020 and September 2021. The modified 8Ds stroke-care algorithm was used for providing patients with timely treatment. Demographic data, risk factors, baseline, and follow-up brain imaging and NIHSS, door-to-needle time (DNT), door-to-puncture time (DPT), complications, and outcome were collected using pre-prepared questionnaires.

Results:: The mean age of the 42 eligible patients for IVT/MTE who are enrolled in the study up until now was 71.4±13.1 years (45.2% male). The most common risk factors were hypertension(69.0%), diabetes(26.2%), and Atrial fibrillation (19.0%). Alteplase was administered for 64.3%, MTE was performed for 11.9% of the patients, and the remaining received bridge therapy. The median baseline NIHSS was 10.5. Median DTN and DPT were 67 and 140 minutes, respectively. In-hospital mortality was 23.8%, and most of them happened in the first week of admission.

Conclusions:: Applying the modified 8Ds helps our institution improve DTN from 76.3 in 2018 to 67 in 2021.
REVERSIBLE POSTERIOR ENCEPHALOPATHY SYNDROM IN THREE CASES

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**Background and Aims::** Reversible posterior encephalopathy is a rare entity whose diagnosis is radioclinical, often it’s associating with headaches, confusion, nausea, convulsions and visual abnormalities; occurring in an acute or subacute manner and often reversible.

**Methods::** We report three cases of posterior reversible encephalopathy observed at the CHU Sétif, Algérie. case 1: BD, 33 years old, presented disturbances of consciousness, convulsive seizures and high blood pressure on a pregnancy. The cerebral CT has shown a bilateral occipital hypodensity and IMR showed to vasogenic edema in the posterior regions in the diffusion sequence. case 2: B.W, 26 years old, BERGER disease with end-stage renal failure and a poorly balanced hypertension. he presented headaches, vomiting, visual disturbances and restlessness with BP: 200/120 mm / Hg. During the examination, we found an HIC syndrome with bilateral blindness. Brain CT revealed bilateral occipital hypodensity, MRI revealed bilateral parieto_occipital anomalies case: 3. S.H, 37 years old, diabetic and hypertensive not followed. She presented headaches with semi-bodily convulsive seizures, BP 220/120, MRI posterior hypersignals. After treatment, 02 patients presented a clear improvement in symptoms, 1 patient kept bilateral blindness.

**Results::** The triggers are multiple, In our observation, hypertension is predominant. Brain MRI is the examination of choice for the diagnosis, showing abnormalities bilateral parieto_occipital vasogenic edema.

**Conclusions::** RPES is a syndrome that is still little understood. Its prognosis can be appalling when it is not recognized and taken care of in time. It is therefore essential to establish effective management in an emergency situation.
Background and Aims:: Shear stress is suggested as one of the mechanism that can cause arterial tortuosity. Pulsatility index (PI) is associated with local shear stress. This study aimed to describe the PI in tortuous internal carotid artery (ICA).

Methods:: This was a retrospective descriptive cross sectional study using the registry of Neurology outpatient clinic, Dr. Cipto Mangunkusumo National Central General Hospital, Jakarta, Indonesia, from January to December 2020. We evaluated the characteristic of subjects with tortuous internal carotid artery according to carotid doppler examination. Univariate analysis, Chi-Square and Independent T-test were performed to evaluate difference statistically.

Results:: There were 129 subjects with mean age of 58±11.22 years. The proportion of ICA tortuosity was 23.2% (30/129). The frequency of tortuous internal carotid artery was significantly higher in women (40.8% vs 13.8%) and dyslipidemia versus non dyslipidemia subjects (40.8% vs 13.8%). Mean of PI, PSV, EDV in tortuous ICA were 1.18±0.30, PSV ICA 73.5±26.6 cm/s, and EDV ICA 24.4±8.5 cm/s, consecutively. There was no mean difference of PI ICA between tortuous and non tortuous subjects (1.18±0.30 vs 1.2±0.35, p=0.43).

Conclusions:: The pulsatility index of tortuous ICA was not significantly different compared to non tortuous subjects. Therefore, vascular risk seemed to have no evidence causing tortuous internal carotid artery in this study.
DEPRESSION AND ISCHEMIC STROKE: DESCRIPTIVE STUDY ABOUT 50 PATIENTS

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Background and Aims:: Post-stroke depression is a frequent complication of stroke with a prevalence ranging from 20 to 60% which justify the importance of a better knowledge of this clinical entity. The aim of this work in to assess the frequency of depressive symptoms and to identify risk factors for the occurrence of depression following stroke.

Methods:: this is a descriptive cross-sectional study conducted at the Neurology consultation of the Mahdia University Hospital, including patients with ischemic stroke of at least 3 months, using a pre-established individual form, the Hamilton score (HDRS) and the Barthel index. Patients with an HDRS score of more than 10 are considered to have depressive symptoms.

Results:: We interviewed 50 patients, 27 men and 23 women with a sex ratio M/F =1.17. The average age was 63 years. 60% had depressive symptoms of which 26% were mild, 56% moderate and 18% severe. The average evaluation time was 14 months ranging from 3 to 24 months. We found no correlation between the severity of depressive symptoms and age of onset, gender, marital status, occupation, length of time since stroke, hemisphere deficit and rate of improvement.

Conclusions:: This confirms the value of surveillance the appearance of mood disorders in the aftermath of a stroke and underlines the benefit of the introduction of antidepressant treatment in terms of functional prognosis and mortality.
HERBAL EXTRACT PREVENTED BRAIN INJURY INDUCED BY CEREBRAL ISCHEMIA-REPERFUSION

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Background and Aims:: Astragalus membranaceus, Scutellaria baicalensis, Phlojodicarpus sibiricus a traditional medicinal herbs, use as adaptogenic, nootropic and vascular remedies in the Oriental medicine. The aim of this work was to verify neuroprotective effect of complex herbal extract composed of Astragalus membranaceus, Scutellaria baicalensis and Phlojodicarpus sibiricus in rats subjected to cerebral ischemia-reperfusion (I/R).

Methods:: Adult Wisar rats were divided into three groups: sham, model and extract groups. Model of cerebral ischemia-reperfusion was induced by 10 min occlusion of common carotid arteries with following reperfusion. The extract was administered to rats intragastrically at a dose of 100 mg / kg once for 7 days before the experiment and 14 days after the occlusion common carotid arteries. Neurobehavioral tests (Neurological Severity Score, rotarod) were performed at 1, 3, 7 and 14 days after operation. Then, the rats were sacrificed and the brain samples were taken for morphological study.

Results:: Compared with the sham group, the scores of neurological were significantly increased, and the indicators on the rotarod test was significantly worse in rats with cerebral I/R (p<0.05). The scores of neurological were significantly decreased, and the residence time on the rotating drum was increased in the treated group compared with the model group (p<0.05). Histopathological study in extract treated rats showing markedly attenuated of neuron death (p<0.05) and arrangement of CA1 neurons as compared with the no treated rats.

Conclusions:: Herbal extract decreased neurological deficites and neuronal damage in rats with cerebral ischemia-reperfusion. The herb extract may be beneficial in the treatment cerebrovascular disorders.

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LDL-CHOLESTEROL AND RISK OF RECURRENT VASCULAR EVENTS IN CHINESE ISCHEMIC STROKE PATIENTS WITH AND WITHOUT SIGNIFICANT ATHEROSCLEROSIS

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Background and Aims:: Recent trials showed that a low-density lipoprotein cholesterol (LDL-C)<1.80mmol/L (<70mg/dL) was associated with a reduced risk of major adverse cardiovascular events (MACE) in Caucasian ischemic stroke patients with atherosclerosis. However, it remains uncertain whether the findings can be generalised to Asians, or that similar LDL-C targets should be adopted in stroke patients without significant atherosclerosis.

Methods:: We performed a prospective cohort study and recruited consecutive Chinese ischemic stroke patients with magnetic resonance angiography of the intra- and cervicocranial arteries performed at the University of Hong Kong between 2008-2014. Serial post-event LDL-C measurements were obtained. Risk of MACE in patients with mean post-event LDL-C<1.80 vs. ≥1.80mmol/L, stratified by presence or absence of significant (>50%) large artery disease (LAD), and by ischemic stroke subtypes, were compared.

Results:: 904 patients (mean age 69±12years, 60% men) were followed up for a mean 6.5±2.4years (mean 9 LDL-C readings/patient). Regardless of LAD status, patients with a mean post-event LDL-C<1.80mmol/L was associated with a lower risk of MACE [LAD+ve: multivariate-adjusted subdistribution hazard ratio (SHR) 0.65, 95% confidence interval (CI) 0.42-0.99; LAD-ve: 0.53, 0.32-0.88] (both p<0.05). Similar findings were noted in patients with ischemic stroke attributable to large artery atherosclerosis (0.48, 0.28-0.84), and in patients with other ischemic stroke subtypes (0.64, 0.43-0.95) (both p<0.05).

Conclusions:: A mean LDL-C<1.80mmol/L was associated with a lower risk of MACE in Chinese ischemic stroke patients with and without significant LAD. Further randomised trials to determine the optimal LDL-C cut-off in stroke patients without significant atherosclerosis are warranted.
REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION EFFECTS ON HEMIPARETIC LIMB SPASTICITY IN STROKE PATIENTS: A DOUBLE BLINDED RANDOMIZED CONTROLLED TRIAL.

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Background and Aims:: Background: Spasticity is known as disabling complications of the stroke interfere with daily activities. Repetitive transcranial magnetic stimulation (rTMS) is an effective technology, safe and non-invasive method of brain stimulation uses in various diseases. This study aimed to evaluated effects of rTMS on spasticity affected upper limb in post stroke patients.

Methods:: This study was a double blind controlled randomized trial. Thirty two patients were randomly allocated in two groups; conservative managements (control group) and (rTMS group) those adding rTMS. The outcome measurement were limb spasticity assessment, Modified Ashworth scale Test (MAST) for dexterity measurement active and passive range of motion (AROM and PROM). All assessments were measured at baseline (T0), immediately after the last session of intervention (T1) and one month later (T2).

Results:: Significant reduction (p<0.05) in outcome reported in the rTMS group in both T1 and T2 as compared with control group.

Conclusions:: It seems rTMS can control muscle spasticity in upper limb stroke survivors and it could be useful for therapists.
THE SOCIAL NETWORK PATTERNS AND PERCEPTIONS OF SOCIAL SUPPORT IN STROKE SURVIVORS

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Background and Aims:: Improving social networks among stroke survivors can improve their recovery and quality of life. However, there is no published baseline data regarding the patterns of social networks among stroke survivors in Singapore. This study aimed to illuminate the social network patterns of stroke survivors in Singapore and the associated satisfaction. It also examined the impact of the COVID-19 pandemic on these variables.

Methods:: A series of questionnaires were conducted online between July 2020 to February 2021. 53 community-dwelling stroke survivors in Singapore were recruited and completed the study (mean age (SD) 60.5 (12.9) years, 27 males). The Stroke Social Network Scale (SSNS) and Multidimensional Scale of Perceived Social Support (MSPSS) were used to assess patterns in social relationships.

Results:: The strength of social networks among stroke survivors was weak and weaker before (49.3±24.2) and during (45.3 ± 23.6) the pandemic respectively. Over half the stroke survivors reported feeling lonely and nearly half reported dissatisfaction with their social relationships, before and during the pandemic. 72.0% of stroke survivors did not belong to any groups in public organisations (e.g. religious groups, trade unions, exercise classes etc), indicating a lack of group membership within wider social networks. Over a third of stroke survivors yearned for greater frequency of contact with their children before and during the pandemic.

Conclusions:: Stroke survivors in Singapore had low levels of social interaction. Strategies increasing stroke survivors’ quality and quantity of social interaction with their children and the community may enhance their quality of life.
HYBERNIA POST-MECHANICAL THROMBECTOMY – ENDOVASCULAR CEREBRAL HYPOTHERMIA TRIAL IN ACUTE ISCHEMIC STROKE (POST-MTECH TRIAL)

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Background and Aims:: Although significant clinical improvement is achieved with mechanical thrombectomy (MT) in large vessel occlusion (LVO) stroke patients, <1/4 patients have outcomes comparable to their baseline (pre-stroke) conditions. Therapeutic hypothermia is a promising method for acute neuroprotection, with multiple beneficial mechanisms, for which a reduction of brain temperature by several °C is required. Systemic hypothermia has been difficult to implement in stroke patients due to the long delay to reach target temperature, complications related to physiological counter-mechanisms to cold, and adverse events associated with whole body cooling. In contrast, targeted brain cooling may provide effective hypothermic neuroprotection, because 1) of more rapid brain cooling (minutes) and 2) it is safer (avoids systemic cooling).

Methods:: This is a multicenter, prospective, randomized, open, blinded endpoint, pivotal clinical trial with an investigational device, a novel endovascular system for selective intra-arterial brain hypothermia, developed by Hybernia Medical, LLC. Eligible patients are LVO stroke patients who undergo acute MT. Main objective is to determine whether selective brain cooling with Hybernia’s device following routine MT in LVO patients results in improved functional outcome (as measured with the modified Rankin Scale) compared to routine MT alone. For this sequential adaptive design clinical trial, up to 1,000 LVO stroke patients will be recruited from 40 international sites.

Results:: Trial description will be uploaded to clinicaltrials.gov in due time. Please contact the authors for more information.

Conclusions:: To determine whether selective brain cooling with Hybernia’s device following routine MT in LVO patients results in improved functional outcome compared to routine MT alone.
IMPACT OF THE COVID-19 PANDEMIC IN THE HOSPITAL CARE OF STROKE

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Background and Aims:: The Covid-19 pandemic had an impact on care and fatality rate from other comorbidities in Brazil. Stroke is one of the main causes of death in the country and early care is essential. To analyze pandemic impact in the first months of installation in Brazil on stroke care, compared to the same period in 2019.

Methods:: Ecological study, with data provided by the Ministry of Health from March to June of 2019 and 2020 and by the Brazilian Institute of Geography and Statistics. The chosen period is based on the beginning of the pandemic in Brazil and the corresponding months of 2019.

Results:: The volume of hospitalizations for stroke in Brazil decreased on average by 5.11% during the pandemic, with the greatest reduction in the Northeast (11.75%), the region with the lowest HDI. The lethality rate increased, on average, 1.48%, mainly in the South (7.5%), the region with the highest HDI in the country. Furthermore, throughout Brazil, despite the average length of stay decreased by 5.06% (mainly in the Northeast, with 7.43% reduction), the average cost per hospital stay increased by 5.11% (mainly in the North, with 7.14% increase).

Conclusions:: A change in important stroke care markers was observed, which may be a consequence of late patient care in health services. Medical care was possibly unstructured due to the pandemic, which may have generated more severe clinical conditions and higher individual costs to the health system.
THE CHALLENGES AND POSITIVE ASPECTS OF INFORMAL STROKE CAREGIVING IN SINGAPORE

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Background and Aims:: Informal stroke caregiving can pose a high caregiver burden on stroke caregivers, however, there is a lack of such data in Singaporean stroke caregivers. This study aimed to investigate the level of caregiver burden and the positive aspects of caregiving experienced by stroke caregivers in Singapore.

Methods:: A series of questionnaires were delivered online between July 2020 to February 2021. 56 informal stroke caregivers (mean age(SD) 52.3(14.2) years, 37 males) completed the study. Measures of strain, competence and burden were assessed by three instruments: Caregiver Strain Index (CSI), Sense of Competence Questionnaire (SCQ) and Caregiver Reaction Assessment (CRA). Participants also commented on positive and negative impacts of caregiving.

Results:: Caregiving burden was high with a mean score of 64.7±27.8 on the CRA. The largest challenges reported by stroke caregivers relate to having limited personal time (51.4%), need to manage expenses of person cared for (43.3%), and having personal health issues from caregiving duties (26.7%). The corresponding strategies deployed by stroke caregivers were seeking support from family on caregiving duties and taking time-off for rest. The most positive aspects of caregiving reported were ability to show filial piety (21.2%, n = 11) and build relationships with family members (21.2%, n = 11).

Conclusions:: This study evidenced the high caregiving burden posed on stroke caregivers, with having limited personal time and needing to manage expenses being the most frequent challenges. Providing respite for stroke caregivers and focusing on positive aspects of caregiving may help to alleviate the caregiving burden.
VARIABILITY OF THE CIRCLE OF WILLIS IN NORTH AMERICAN CAUCASIAN AND MIDDLE EAST ARABIC COHORTS

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Background and Aims:: The cerebral arterial circle (circle of Willis) plays an important role in the redistribution of the blood flow between the anterior and posterior territories and maintains the plasticity of the cerebral blood circulation. The heritability and prevalence of certain variants of the circle of Willis in different ethnic and racial groups are frequently disputed by authors.

Methods:: Our cross-sectional retrospective study aims to compare the patterns of the cerebral arterial circle in 64 Caucasian cadavers with 64 Arabic living individuals, by methods of anatomic dissection and magnetic resonance angiography, respectively.

Results:: The typical structure of the circle of Willis was revealed in 8.3% of the Caucasian study group, and in 22.2% of the Arabic one. The anterior part of the circle of Willis was incomplete in 6 out of 64 of the Caucasian specimens, where the anterior communicating artery was hypoplastic (6.3%) or absent (3.1%). The posterior part of the circle of Willis had a hypoplastic or absent posterior communicating artery on one side in 20, and on both sides in 12 out of 64 Caucasian specimens. In the Arabic cohort, the posterior part of the circle of Willis was incomplete in 17 out of 64 specimens, with the absence of the posterior communicating artery unilaterally (in 11 cases) or bilaterally (in 6 cases).

Conclusions:: The present study reveals that the configuration of the cerebral arterial circle and distribution of the blood flow between the anterior and posterior territories have certain differences in the Caucasian study group versus the Arabic one.
A CASE REPORT OF A BILATERAL THALAMIC HEMORRHAGE

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Background and Aims:: Intraparenchymal hemorrhages (IPH) are responsible for 6.5% to 19.6% of all stroke cases. Primary simultaneous IPH are responsible for 0.7% to 3% of intracerebral hemorrhages. Unilateral thalamic IPH are infrequent and even more rare when the presentation is bilateral. Our aim is to present a rare bilateral thalamic hemorrhage case.

Methods:: Case report of a 53-year-old female presenting with headache and left hemiparesthesia, followed by loss of consciousness. The patient arrived at our department with global aphasia, left hemineglect, photoreactive pupils, and left lip deviation. Her arterial pressure was at 210/110 mmHg.

Results:: Cranial CT was performed, which evidenced bilateral foci of intraparenchymal hemorrhages in the thalamus. The intracerebral hematoma appeared to compress the third ventricle, with subtle dilatation of the lateral ventricles, but there were no signs of intraventricular bleeding, nor hidrocephalus. There was no significant midline deviation. In consequence of clinical deterioration and consciousness loss to eight according to the Glasgow Coma Scale, management included orotracheal intubation, transference to the ICU, and mechanical ventilation, associated with intensive management of the arterial pressure. During hospitalization, the patient contracted infections, which were resolved through antibiotic therapy. Finally, gastrostomy was performed for hospital discharge.

Conclusions:: We describe a patient with important impairment, which can have been worsened by the acquired infections, a significant cause of mortality. To our knowledge, only five other cases of bilateral thalamic IPH were reported in Latin America, none of them in Brazil. This is the youngest woman reported in Latin America with bilateral simultaneous thalamic IPH.
Background and Aims:: Cranioplasty after DC is commonly use as the treatment for medically refractory intracranial hypertension in cerebral trauma, SAH, ICH, Tumors, where it is better studied, but also in malignant stroke(1). Even in Stroke the aims of the cranioplasty are protection of the brain, restoration of the brain's hydrodynamic conditions and cosmetics, determining a clinical outcome improvement comprehensive of neuropsychological function(2). Cranioplasty can be performed by using autologous bone or alloplastic materials and timing of cranioplasty seems to be related to the clinical outcome and it should be performed after 90 days from DC(3). Cranioplasty complications are sepsis(5%), Hematoma(19%), Sieroma(6,2%), pneumocefaus(4%), hidrocefalus(2%) and fractures(1%) but the available studies include mainly cumulative results of the illnesses previous indicated. The aim of our work is to study timing and complications of cranioplasty in a cohort of MCA malignant stroke.

Methods:: All patients with malignant MCA infarction undergone to decompressive craniectomy in Modena-Stroke Unit between January 2015 and June 2021 were evaluated. Clinical features -including mRS at 3 and 12 month follow up-, neurosurgical and neuroradiological parameters were collected.

Results:: We evaluated a total of 31 patients presenting preliminary results; 8 of them had second cranioplasty because of major complications. 12 interventions of 39 were performed with heterologous bone flap. The median time of the intervention was 186 days, and also excluding the second cranioplasty is about 162 days.

Conclusions:: Cranioplasty in patients with malignant MCA infarcts submitted to DHC is a delicate intervention affecting the clinical outcome that need specific studies.
INFLUENCE OF MULTICOMORBIDITY ON THE RESPONSE TO THROMBOLYSIS IN ISCHEMIC STROKE

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Background and Aims:: Introduction: Thrombolysis has a high level of evidence in ischemic stroke, in which reperfusion may depend on the patient's clinical condition. The Charlson Comorbidity Index (CCI) measures the degree of comorbidities, having a prognostic value in post-stroke. Objective: Evaluate the influence of multicomorbidity on thrombolysis reperfusion in stroke patients.

Methods:: Prospective cohort of patients admitted to stroke unit between 2017 and 2020. Multicomorbidity was defined as Goldstein-modified CCI ≥ 2 points. Patients were compared for reperfusion to thrombolysis, functional disability or death at 90 days (mRS>2). Reperfusion due to thrombolysis was defined as NIHSS ≤1 or reduction ≥8 until hospital discharge.

Results:: 165 individuals were included, the mean age was 60.5 (±15.9) years. Median NIHSS at admission was 10 (7-14). Prevalence of multicomorbidity at admission was 24.1%. No difference was found comparing groups for reperfusion to thrombolysis [45.7% vs 45.8%, RR = 0.99 (95%CI 0.66 - 1.51)] and functional disability or death at 90 days [41% vs 37.5 %, RR = 1.09 (95%CI 0.70 - 1.70)]. In the multivariate analysis, multicomorbidity was not associated with worse outcomes, whether mRS>2 at 90 days [aOR = 0.76; (95% CI 0.30-1.87)] or insufficient response to thrombolysis [aOR = 0.92; (95% CI 0.40-2.14)], adjusted for age, NIHSS at admission, length of hospitalization, ASPECTS and occurrence of delirium.

Conclusions:: Conclusion: Presence of multicomorbidity was not associated with a lower response to thrombolytic treatment or greater functional disability 90 days after stroke. Our results suggest that the prognosis may be favorable in multicomorbidity patients undergoing thrombolysis.
REPERFUSION STRATEGIES IN ACUTE ISCHAEMIC STROKE: OUR EXPERIENCE AND FUTURE THERAPEUTIC PROSPECTS

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Background and Aims:: Thrombolysis is the approved treatment of the acute ischemic stroke, not always successful, the aim is understanding the ischemia pathophysiology to suppose adjuvant therapies. Methods:: 223 patients (pts.), referred to the Emergency Department, underwent intravenous thrombolysis (IV-TL) and/or endovascular treatment (EVT). Results:: 147/223 (65.9%) pts. received IV-TL; 76/223 (34%) pts. isolated EVT (42%) or associated with IV-TL (57.8%); 30 pts. (39%) exhibited complete (TICI 3) and early recanalization. Favourable outcome at three months (0-2 mRS) in 137/223 (61.4%) pts., moderate (mRS: 3) in 21/223 (9.4%) pts., unfavourable in 66/223 (29.5%) pts. Poor prognostic factors: TACS, severe atheromasia, poor collateral circulation, more complications. Positive prognostic factors: good primary collateral circulation and higher Careggi Collateral Score; higher TICI grade (p<0.005); faster procedure (p<0.001); effective lysis or compensation-induced recanalization (p< 0.005). Concerning subjects receiving EVT treatment the best outcome was obtained with associated treatment (30/44 pts. – 68%), compared to isolated treatment (9/32 pts. – 28%). Conclusions:: Reperfusion is achieved through thrombolysis and/or collateral flow with a better outcome when both events occur. Ineffective congenital collateralization or macro and microcirculation damage may impair any compensation, thus being able to prevent reperfusion and trigger reocclusion. This study highlights that, while providing satisfactory results, in subjects undergone EVT especially evident in bridging pts., the above strategies are not always successful. Therefore additional therapies should be considered using alternative thrombolitics, enzymes.
DECOMPRESSIVE HEMICRANIECTOMY (DH) IN MCA MALIGNANT INFARCTION: FIRST FINDINGS IN MODENA REGISTRY ABOUT CLINICAL AND NEURORADIOLOGICAL PROGNOSTIC INDICATORS.

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Background and Aims:: DH in MCA malignant stroke has been demonstrated to reduce mortality over 50% in the acute phase, determining an increase in moderate-to-severe disability in the surviving patients, as compared to patients receiving medical treatment. In this preliminary analysis we want to evaluate clinical and neuroradiological prognostic indicators in patients with malignant cerebral infarction treated by DH.

Methods:: This is a single center registry of MCA malignant infarction treated by DH. Anamnestic, clinical, timing and neuroimaging pre and post intervention characteristics were collected. Follow-up assessment by mRS was at 3 and 12 months after surgery.

Results:: A total of 59pt were registered between September 2008 to June 2021. Comparing the data of the clinical outcome at 1 year with those of a pooled analysis of three European randomized clinical trials (HAMLET, DECIMAL, DESTINY I), the overall mortality of our group was higher (28.3% vs 22%), especially in case of late intervention (>48h), low GCS (<10), high volume of the ischemic lesion (>400cc), brain midline shift >10mm and additional ischemic involvement of ACA or PCA territory. Among the survivors our patients presented clinical outcomes similar to the trials one (mRS=3: 27% vs. 29%; mRS=4: 35% vs. 31%).

Conclusions:: DH in the treatment of malignant brain infarcts has changed the natural history of this disease in terms of mortality and functional outcome. Our study showed that late intervention, low GCS, high volume of the lesion (>400cc), brain midline shift >10mm and additional ischemic ACA and/or PCA involvement are associated with a higher mortality.
BACKGROUND AND AIMS:: IAD is an uncommon and underdiagnosed disease, the aim is to identify its pathophysiological mechanisms and possible alternative therapies.

METHODS:: Eight patients (pts.), referred to the Emergency Department with focal signs, were analyzed. Work-up: neurological examination, brain CT-MRI/AG, Digital-Angiography (DA) and Ultrasound.

RESULTS:: All pts. were diagnosed with cerebral ischemia. AG highlighted intradural internal carotid artery (ICA) dissection in three pts. and both intra- and extracranial ICA dissection in one pt. In one subject subarachnoid haemorrhage from rupture of intradural ICA dissecting aneurysm, treated with embolization, was observed; in another pt. dissection of the basilar artery (BA) was detected, whereas the other pts. were found to have vertebral artery dissection (VAD). Four pts. were given Actilyse, followed by mechanical thrombectomy (MT) in two subjects; one pt. underwent only BA MT. The thrombolytic was administered in all pts. with confirmed diagnosis of vessel occlusion prior to the dissection finding. Subsequent or alternative therapy was aspirin. The three-month outcome was good in all pts.

CONCLUSIONS:: The thrombolytic therapy has not caused bleeding in the small sample of examined pts., thus suggesting that it acts on the thrombotic process, without affecting the integrity of the vessel wall, although the latter is poorly equipped with elastic fibers and easily vulnerable to any noxa, probably more traumatic than pharmacologic. The study of these few cases provides elements to reflect on alternative therapeutic options that could envisage, after large retrospective studies and specific trials, the use of thrombolysis also in intracranial vessels dissections.
CONTINUING TRAINING AS THE MAIN FACTOR FOR IMPROVE OUTCOMES IN A
COMPREHENSIVE STROKE CENTER IN A DEVELOPING COUNTRY

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Background and Aims:: Building protocols in developing countries as good as in developed countries is a different story. The treatment centers present dissimilar conditions; their infrastructure is often inferior to those in developed countries, and the healthcare models are usually deficient.

Methods:: In this retrospective observational study, medical records of all patients undergoing treatment with endovascular techniques at a Mexican hospital that implemented a mechanical thrombectomy for LVO program (stroke program) were reviewed. The selection began in February 2017 and ended in January 2020 (36 months).

Results:: Thirty-six months was the length of total data collection, which was grouped into periods of 6 months each. These groups were compared with each other, taking the 90-day mRS, the total time used in the algorithm, and the recanalization time as variables. The recanalization time had statistical significance with its decrease in the last 18 months (p = 0.035). The temporal midline was set at month 18 (July 2018). During the first 18 months, 17 (23%) patients had favorable outcomes (mRS <3), whereas in the last 18 months (second half), 45 (33%) patients with good clinical outcomes (mRS <3) were found (p = 0.0001).

Conclusions:: With logistic adaptation, creativity, but above all, permanent training, similar results to those in other parts of the world can be achieved.
LONG-TERM OUTCOMES AMONG NIGERIAN STROKE SURVIVORS; DATA FROM THE COGFAST-NIGERIA STUDY

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Background and Aims:: Africa faces a rising burden of stroke with rising incidence and prevalence but little is known about the profile and trajectory of long-term outcomes and mortality after stroke. The aim of this study is to explore the trajectory and determinants of long-term outcomes up to four years among a cohort of stroke survivors recruited into the CogFAST-Nigeria study.

Methods:: The data were collected in a longitudinal study of stroke survivors who were prospectively recruited from the FMC Abeokuta and UCH Ibadan Nigeria. Cognitive function was measured using the vascular neuropsychological battery, depression was measured by the GDS-short form, functional dependency through the Barthel Index. Baseline enrolment was 3 months after stroke (2009-2010) and the stroke survivors were followed up for a period of four years after the baseline enrolment.

Results:: 253 stroke survivors were recruited into the study, 157 (59.7%) were males and mean age was 60.2 (±/-9.8) yrs and mean yrs of education was 10.36 (±/-4.9). The proportions with cognitive impairment were 53.2% at six months follow-up, 56.9%, 58.7%, 60.9%, and 66.7% at 1, 2, 3 and 4 years, while the proportion of those with depression were 39.3% at 3 months post-stroke, 35.2%, 35.5%, 26.7%, and 36.1% at 1, 2, 3 and 4 years. The case fatality rate was 7.5% (95% C.I = 4.82-11.4) at 6 months post-stroke, 24.8% (95% CI = 19.93-30.6), 39.4% (95% CI=3.65-45.7) and 45.3% (95% CI=39.42-51.6) at 1, 3 and 4 years follow-up.

Conclusions:: There is a need to improve stroke rehabilitation among stroke survivors including particular attention on those with recurrent stroke.
**BLOOD PRESSURE IS ASSOCIATED WITH SEVERELY LOW ADL AT HOSPITAL DISCHARGE AFTER ATHEROTHROMBOTIC INFARCTION: A RETROSPECTIVE CROSS-SECTIONAL STUDY**

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**Background and Aims::** We analyzed inpatients’ data, and investigated the effect of blood pressure on outcomes of rehabilitation after atherothrombotic infarction.

**Methods::** This retrospective cross-sectional study analyzed the data obtained from the Japan Association of Rehabilitation Database. We excluded inpatients with a past medical history of cerebrovascular diseases (CVDs) or different types of CVDs, and those without records of hypertension or Barthel Index (BI). We compared activities of daily living (ADL) between hypertensive and non-hypertensive inpatients using 10 BI activities and the total BI score at hospital discharge. BI activities were dichotomized into independent population (patients with the highest score for each activity) and their non-independent counterparts.

**Results::** Three hundred and thirty-six patients with atherothrombotic infarction were analyzed; 225 were hypertensive and 111 were not. Non-hypertensive condition was associated with high dependency of BI activities; feeding, transfers, toilet use, dressing, bowel control, and bladder control. The total BI score of hypertensive patients at discharge was higher than that for their non-hypertensive counterparts (BI 0–15 versus 20–100, \( P = 0.0003 \); BI 0–35 versus 40–100, \( P = 0.0224 \), non-continuous variables).

**Conclusions::** BI activities were used to analyze the outcome of atherothrombotic infarction after rehabilitation. Hypertension has protective effect on severely low ADL at discharge.
RELATIONSHIP OF TOOTH LOSS TO MILD COGNITIVE IMPAIRMENT AMONG MIDDLE-AGED MONGOLIANS: MON-TIMELINE STUDY

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Background and Aims:: Cognitive impairment is common in elderly people, which is why it is considered an aging disorder. However, cognitive decline – including dementia – can also occur in middle-aged people. Cognitive impairment is caused by multiple risk factors. We hypothesized that tooth loss may also be a potential risk factor among Mongolians, as oral health problems are one of the major health issues in Mongolia, especially in middle-aged people.

Methods:: In this cross-sectional study, we used the baseline data from the Mon-Timeline cohort study, including people older than 40 years of age (n=291). The amount of tooth loss was assessed by a trained researcher. Mild cognitive impairment (MCI) was defined as those participants scoring a total of £24 points on the Mini-Mental State Examination (MMSE).

Results:: Unadjusted analysis showed that having more tooth loss (>10) increased the risk of MCI by an Odds Ratio of 3.03 (1.49-6.17), as compared with having less tooth loss (£10). The association remained significant even after adjusting for covariates, suggesting that tooth loss is associated with MCI risk, independent of age, education and other socioeconomic factors. We tested the interaction effect of age and found that there was no significant interaction effect of age in the association between tooth loss and MMSE scores.

Conclusions:: In conclusion, tooth loss may play a role in the development of cognitive decline, especially in the early onset of dementia. Further studies are needed to investigate whether early tooth loss at younger ages is associated with dementia, especially in middle-aged people.
SPHENOID RIDGE MENINGIOMA PRESENTING AS ISCHEMIA STROKE

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Background and Aims:: Background : Ischemic stroke as the presenting feature of sphenoid ridge meningioma is extremely rare.

Methods:: Case Presentation: A 49-year-old woman presented with acute onset of left hemiparesis, dysarthria and left central-type facial palsy. Magnetic resonance imaging (MRI) with angiography (MRA) confirmed the presence of an extra-axial mass in the medial portion of the right sphenoid ridge that compressed and distorted the first segment of the right middle cerebral artery (MCA) postero-superiorly, thereby resulting in an acute cerebral infarction in the right MCA territory. Cerebral angiography demonstrated stenosis of the right proximal M1 portion.

Results:: Case Presentation: The patient underwent simpson grade III resection through the pterional approach, the vessel compression was resolved. The pathology revealed a meningothelial meningioma. She was maintained on oral aspirin at 160 mg/ day, after a 6-month rehabilitation programme, the patient recovered with mild paresis in the left upper extremity.

Conclusions:: Conclusion: We present a well documented case of sphenoid ridge meningioma causing acute cerebral infarction as a result of middle cerebral artery compression. Even it is extremely rare, the possibility of sphenoid ridge meningioma must be considered in the differential diagnosis in patients with acute infarction.
SUCCESSFUL SURGICAL MANAGEMENT OF A TENTORIAL DURAL ARTERIOVENOUS FISTULA CAUSING SPINAL CORD MYELOPATHY

Hatim Belfquih
Avicenne hospital Marrakech, Neurosurgery, Marrakech, Morocco

Background and Aims:: Background: Intracranial dural arteriovenous fistulas account for 10 to 15% of all intracranial arteriovenous malformations. Tentorial dural arteriovenous fistulas with spinal medullary venous drainage causing spinal cord myelopathy have been rarely reported in the literature. We describe a case using a temporo-pterional approach for the surgical treatment of a tentorial artery dural arteriovenous fistula causing spinal cord myelopathy.

Methods:: Case presentation: A 48-year-old male presented complaining of a 15 days history of incoordination and dizziness and from 2 days history of progressive heavy weakness of his upper and lower limbs with bowel and bladder incontinence. The patient had magnetic resonance imaging (MRI) performed along with cerebral and spinal angiography that revealed a left tentorial artery dural arteriovenous fistula with spinal medullary venous involvement down to T6.

Results:: Case presentation: Angiographic embolization was attempted, but selective catheterization was unsuccessful. The patient underwent a temporo-pterional approach with obliteration of the dural arteriovenous fistula. The post-operative angiogram confirmed complete obliteration of the dural arteriovenous fistula.

Conclusions:: Conclusion: Intracranial dural arteriovenous fistulas are a rare cause of spinal cord myelopathy. When a patient presents with suspicion of spinal dural fistula and negative spinal angiography, an intracranial origin should be suspected and a cerebral angiogram performed. Skull base approaches along with intraoperative angiography provide an alternative modality for obliteration of the dural arteriovenous fistula nidus, thereby eliminating the venous congestion and hence the spinal cord ischemia.
COVID-19 LOCKDOWN AND TELE-EDUCATION TOOLS AT A NEUROLOGY RESIDENCY. A QUASI-EXPERIMENTAL STUDY

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Background and Aims:: COVID-19 is an infectious disease caused by the SARS-COV2 virus discovered in 2019. Since its detection in Wuhan-China, it has spread all over the world causing emergency lock-downs in many countries. Mexico declared national emergency in March leading to disruption of neurology training programs at the National Institute of Neurology and Neurosurgery (INNN). This study aims to evaluate Tele-educational interventions implemented to continue those programs.

Methods:: This is a quasi-experimental study. Sample population of Neurology residents consisted of 23 trainees. The intervention was a Headaches’ Tele-educational module. Diagnostic and final tests were conducted to assess resident’s improvement. Primary outcome was improvement in headaches’ knowledge measured by the change in grades. Residents of each year were evaluated separately as secondary outcome.

Results:: Mean initial score was 67.02 (SD +/- 20.17) while mean final was 78.64 (SD +/- 9.21). Showing a difference of +11.62 points [CI 4.31-18.9 p 0.003]. (Figure 1)

First-year resident’s showed a median difference of 18.05 points (CI [4.165-31.915] p= 0.013) while second-year residents showed 4.125 points difference(CI [0.0001-6.940] p=0.044). The residents who improved the most were 1st-year. (Figure 2)
The performance in each item-category was measured. The lowest improvement was observed in the “Treatment” category while “Physiopathology” showed the highest. Significant improvement in all categories was observed (p=0.028). (Figure 3)
Conclusions:: In conclusion, Tele-educational interventions showed promising results when evaluating neurology residents' knowledge. But a proper control group and longer evaluating times are lacking. However, these results show that the change in paradigm can be applied to more topics without sacrificing neurological learning objectives.
Background and Aims:: Neurophobia is the fear of neuroscience and clinical neurology, inability to utilize the basic neurological knowledge at the bedside. Most of the general practitioners display less confidence when dealing with neurological cases. The exact reasons for neurophobia are not well known and it likely as a result of multiple contributory factors. Our study aimed to assess the attitude toward Neurology and to explore the reasons for this attitude.

Methods:: A self-administered, previously validated questionnaire was distributed among 393 students and interns in Sudan from July 2020 to February 2021. In this cross-sectional study, the questionnaire included demographic data and 12 statements to examine attitudes toward neurology using a Likert scale.

Results:: Participants’ mean age was 25.5 years. The students constituted 56.2% of the study population. 53% of our participants were not considering neurology as a future career. Almost 9% strongly agreed that difficulty to elicit signs in neurology is a barrier from taking neurology as a career, while 16.5% disagree that neurology has limited treatment. Most importantly, the long training time in neurology and the emotional difficulty in taking care of patients was the most cause of preventing participants from pursuing a neurology career (54% and 34% respectively). Higher number of students consider neurology as career when compared to interns (p value = .003). In addition, when compared neurology difficulty among occupations groups, medical officer was the most category that consider neurology difficult (p value = .014).

Conclusions:: Neurology was perceived as a difficult medical specialty and the reasons behind this attitude is wide ranging.
NEUROPHOBIA AMONG MEDICAL STUDENTS IN SUDAN

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Background and Aims:: To describe factors that contribute to students’ perception towards neurology, and their views on how to improve neurology training.

Methods:: A cross-sectional computerized survey was conducted among 171 medical students from Bahri University, Sudan, in the period from 8th, January 2018 to 30th, January 2018. The questionnaire included demographic data and 16 statements to assess: their neurology teaching experience, factors that would drive them toward or away from neurology, and their views on how to improve neurology training at their medical school.

Results:: Females constituted 87.7% of participants. The mean age was 21.93 (SD +/- 1.24) years. The majority of participants (83%) were not decided on their future career, and 31% of them stated that they would not consider neurology as a career. Almost half of medical students considered neuroscience and neurology teaching unsatisfactory (46%). More than half (56.8%) found neuroanatomy as well as neurological diagnosis to be contributing to neurology being perceived as a difficult subject. Of Our participants, 60% though that there are limited treatment in neurology, and 46% considered neurology outcome to be poor. Among the participants, 64.9% thought that neurology as a career choice provides good financial reward and 85.9% thought that it provides good research opportunities. Most students thought that better lectures (80.7%), better bedside teaching (82.5%), and longer time schedules allocated to neurology (90.7%) would improve their neurology training.

Conclusions:: Although there is generally unfavorable behavior towards neurology among our studied group, there was a large percentage that would consider it as a career.
EDUCATIONAL STRATEGIES IN A NEUROLOGICAL-NEUROSURGICAL FACILITY: VIRTUAL COURSE IN ENCEPHALIC VASCULARIZATION

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Background and Aims:: Educational challenges in tertiary, neurological-neurosurgical facilities involve keeping staff updated, while holding firmly to the basic tenets. Knowledge of encephalic vascularization is essential to all in this scenario. Objective :To describe the creation of an online course on encephalic vascularization

Methods:: HPS-IMIP/SES/SUS has a customized educational platform (“Pelopidas Digital” Virtual-Teaching-Platform (PD-VTP) designed to provide short, point-of-care video-tutorials and tests on subjects of interest to Unit's personnel. PD-VTP is available through intra/internet (pelopidasdigital.imip.org.br). The basic unit of the PD-VTP is a module, formed by a) introduction, b) learning objectives, c) 05-minute tutorial video/video-text, d) test and e) recommended reading. Modules can be grouped into courses. The virtual course “Encephalic Vascularization” was created following Tutorials and Guides of Board of Teaching and Research HPS.

Results:: Three domains of knowledge were considered for virtual training in cerebral vascularization: 1) Anatomo-radiologic correlation of arteries and, 2) Veins and venous sinuses, 3) Clinical implications.

Conclusions:: Creation of a virtual course on cerebral vascularization is an attractive tool for dissemination of knowledge. It may involve trainees as tutors once familiar with the technological tools and supported by institutional educational teams. Health education in digital learning environments such as PD-VTP 1) accelerates training of members of therapeutic team, 2) allows for periodic audits and certification, 3) is unlimited in amount of times professionals can consult its contents and may 4) engage trainees and staff members as tutors, involved in creating virtual tools for education in neurology.
COGNITIVE AND PSYCHO-EMOTIONAL DISORDERS IN PERSONS WITH FUNNEL CHEST DEFORMATION

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Background and Aims:: Funnel chest deformation (FCD) is a manifestation of connective tissue dysplasia. The aim of our study was to identify the nature of some disorders of higher nervous activity under this pathology.

Methods:: 43 patients with FCD were examined within the preoperative period. We used the following scales: Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and Hospital Anxiety and Depression Scale (HADS).

Results:: The mild cognitive impairments were found in 12 patients (57%), moderate ones in 6 patients (29%) and 3 patients (14%) had no abnormalities in the psycho-emotional sphere. These disorders were more pronounced in persons with FCD of the II and III degree. The mean values of the MMSE and the MoSA decreased in persons with mild cognitive impairments. The mild modal-nonspecific mnestic disorders were observed. The largest number of errors occurred when naming date and reproducing the unrelated words, both directly and delayed. The direct reproduction of the memorized material was especially decreased. The decrease in intellectual flexibility was also noted in persons of the II degree. According to the HADS data, there was an increase in the incidence of anxiety and depression in most of the examined patients, especially in persons of the II degree. The signs of clinically severe depression were found in 2 patients (10% of examined persons). The subclinical depression was detected in 11 patients (52% of examined persons).

Conclusions:: The anxiety-depressive emotional disorders predominated in persons with funnel chest deformations, and they were combined with mild cognitive impairments in the vast majority of patients.
OBJECTIVE INDICATORS OF VISUAL EVOKED POTENTIALS IN CHILDREN WITH COGNITIVE IMPAIRMENTS

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Background and Aims: Cognitive impairments are an urgent problem in neurology. The impairment of cognitive activity leads to learning difficulties, deviant behavior, psycho-emotional disorders and, as a consequence, social maladjustment and a decrease in the child’s quality of life. Purpose: to assess the degree of cognitive impairments in children using VEP.

Methods: Materials and methods: we examined 65 children in two groups: Group 1 - 30 children with mental retardation, Group 2 - 35 children with ADHD. The VEP technique was applied to all the children. We measured the peak latency of the waves (PL) – the time from the moment of the stimulus onset to the top of the wave, which characterizes the velocity of the impulse conduction through the visual analyzer. In children of Group 1, the peak latency of the P1 component was 59.3 m/s (N = 68.9), which indicated a decrease in the impulse conductance through the visual analyzer at the level of the cerebral cortex. The peak latency of the N1 wave in Group 2 was 83.0 m/s, (N = 72.0), which indicated a violation of the connections between the subcortical system and the cerebral cortex.

Results: In applying the VEP technique, reliable results were obtained, which should be taken into account in the differential diagnosis of ADHD with delayed psychological development.

Conclusions: An increase in VEP latency indicates a slowdown in the conduction of a nerve impulse at different stages of the visual analyzer, which can serve as an additional diagnostic criterion in assessing cognitive functions in preschool children.
Background and Aims:: Our study was aimed at studying cognitive impairments in children with mental retardation and children with attention deficit hyperactivity disorder (ADHD), using psychological testing validated in the Republic of Uzbekistan.

Methods:: We examined 60 children in two groups: Group 1 - 30 children with ADHD, and Group 2 - 30 children with mental retardation. The psychoneurological status was assessed through evaluation of memory, thinking, perception, attention, psychoemotional, speech sphere, gnosis and praxis. In psychological testing of cognitive processes, the analysis of testing was assessed using a point-based system. It should be noted that the methods of psychological testing (S.P. Glukhova, R.I. Sunnatova) have been adapted and validated in Uzbekistan. We assessed their significance in the course of providing outpatient care to children. To study perception, memory, thinking, and attention, “Who is Hidden in the Pictures?”, “10 Things”, “Pre-Cut Pictures” and “Correction Test” techniques were used.

Results:: The analysis of testing in children with ADHD showed a moderate decrease in the level of attention and perception, with the preservation of thinking and memory processes.

Conclusions:: The overall score was 30-32 points (high level of development). The assessment of the psychological development of children with delay in psychoverbal development was 12-16 points, which indicated a low level of cognitive processes (memory, thinking).
THE PREVALENCE OF NEUROLOGICAL SYMPTOMS & PSYCHIATRIC MANIFESTATIONS OF TETRAHYDROCANNABINOL (THC) AMONG CANNABIS USERS IN PSYCHIATRIC FACILITIES IN KHARTOUM STATE, SUDAN 2021

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Background and Aims:: Cannabis refers to three group of plants with psychoactive properties. It can contribute to wide range of neurological and psychological manifestations. To study the prevalence of neurological symptoms & psychiatric manifestations of tetrahydrocannabinol among cannabis users in psychiatric facilities.

Methods:: This is an observational analytical cross sectional hospital based study that was conducted at psychiatric clinics in three hospitals in Khartoum state among 34 adults chosen as total coverage for 4 weeks, using The Edinburgh Neuro-symptoms Questionnaire, Mini international neuropsychiatric interview 5th edition and DSM-V.

Results:: All of the 34 were males, the mean age was 27.53 years. All of the users have psychiatric symptoms (bipolar disorders 29.4%, OCD 41.2%, psychotic feature 35.8%, major depressive disorder 67.6%, anxiety-like symptoms 61.8%, social phobia 44%, panic attack 38.2%, ideation of suicidality 47.1% and 23.5% planned to suicide). The 34 have neurological symptoms (17.6% experienced loss of consciousness (20.6% of them had convulsions), status epilepticus 11.8%, limb weakness 32.4%, numbness and altered sensation 29.4%, memory problems 64.7%, fatigability 58.8%, tremor 26.5%, lack of concentration 52.9%, blank spells during the day 47.1%, pain almost every day in more than one part of the body 29.4, vision disturbance 35.3%, tinnitus 14.7%, difficulty in swallowing and feeling of something stuck in the throat 11.8%, difficulty in speaking 35.3% and 11.8% had stutter at age of 16).

Conclusions:: The issues of cannabis should be taken seriously, because it is a great contributor to wide range of neurological and psychiatric manifestations.
A PHASE 2, DOUBLE-BLIND, PLACECO-CONTROLLED STUDY OF THE SAFETY AND EFFICACY OF MICROBIAL ECOSYSTEM THERAPEUTIC-2 (MET-2) IN PATIENTS WITH MAJOR DEPRESSION: PROTOCOL AND PRELIMINARY RESULTS

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Background and Aims:: Introduction: Recent studies have investigated the potential of treatments that modify the gut microbiome, such as fecal microbiota transplantation (FMT) and probiotics, in individuals with psychiatric illnesses. The aims of this double blind randomized controlled trial was to investigate the safety and efficacy of a novel gut microbiome therapeutic, Microbial Ecosystem Therapeutic-2 (MET-2), in people with depression.

Methods:: In this trial, sixty adults diagnosed with Major Depressive Disorder will be recruited. Participants will consume orally once daily an encapsulated microbial therapeutic, containing 40 strains of bacteria purified and lab-grown from a single healthy donor stool, or a placebo alternative for 6 weeks. Participants will be assessed on a biweekly basis in order to evaluate the safety and efficacy of the therapeutic using clinical scales and questionnaires.

Results:: Findings: The therapeutic has been found from earlier studies to be generally safe and tolerable, with limited adverse events and side effects, and no serious adverse events. We expect participants' mood symptoms to improve over the course of their involvement in the study as a result of changes in their gut microbiome composition and immune marker levels.

Conclusions:: The findings of this study will be the first to provide evidence for the role of microbial ecosystem therapy in treating depression in comparison to a placebo alternative.
FUNCTIONAL NEUROLOGICAL DISORDERS MIMING A STROKE: MANAGEMENT IN THE ACUTE PHASE

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Background and Aims:: The prompt recognition of stroke symptoms is mandatory in the emergency department (ED) in line to guarantee the right acute reperfusion therapy. Intravenous thrombolysis remains the first line therapy suggested, it may consent vessel recanalization and neurological deficit regression. Stroke mimics (SM) can account for up to 25% of all acute stroke presentations. Among stroke mimics functional neurological disorder are increasing overtime. The rate of false-positive diagnoses of ischemic stroke, "stroke mimic", ranges from 1.3% to 25% in patients not treated with thrombolysis.

Methods:: In our retrospective analysis we isolated 24 patients suffering of a functional neurological disorder that were admitted in our Stroke Unit for a sudden focal neurological deficit.

Results:: All patients with functional neurological disorder were first evaluated in the ED, than admitted in our Stroke Unit, in 9 cases thrombolysis was performed and was safe. In line with previous studies, patients with functional neurological disorder were young, mostly with family or personal history of neurological and psychiatric pathology.

Conclusions:: In the ED is quite difficult to discriminate a stroke from a psychogenic stroke mimic but physicians have to decide in a short period which treatment start quickly. Thrombolysis is safe in SM. We describe the experience of our stroke unit in the recognition and management of acute neurological deficit due to functional neurological disorder. More data are required to draw up a right diagnostic protocol that may guide clinicians in the proper selection of patients that would benefit from thrombolysis.
THE EFFECT OF BRAIN GYM TOWARDS ANXIETY LEVEL OF ELDER PEOPLE IN RURAL AREAS OF YOGYAKARTA, INDONESIA

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Background and Aims:: In 2012 The National Statistical Committee of Indonesia stated that the number of elder people in Yogyakarta was at 13.04% of all Indonesian populations. The elder people need more attention and safe medications which may affect their physical and psychological bodies. Some elder people may suffer from any emotional imbalance, including anxiety or mood disorders. The prevalence of anxiety in individuals 55 years old or more is 2.8%. One of the effective ways to control and maintain the emotional level is a brain-stimulating activity or known as brain gym. This study aims to find out the effect of brain gym on the level of anxiety in elder people in the rural areas of Yogyakarta, Indonesia.

Methods:: This was a community-based analytical study with quasi-experimental and using pre and post-test one-group design. The level of anxiety was measured with Hamilton Anxiety Rating Scale (HARS) before and after the brain gym. The brain gym was performed on each respondent for 2 months with the duration of each session was 30 minutes every twice a week.

Results:: The results from 26 respondents were that the mean score of HARS before brain gym was 9.38 ± 6.01 or categorized as mild anxiety. After brain gym for 2 months, the mean score of HARS was 5.12 ± 5.24 or categorized as no anxiety. The results also showed that brain gym had the significant effect of lowering the level of anxiety (p=0.006).

Conclusions:: Brain gym had a significant effect on lowering the level of anxiety of elder people in rural areas of Yogyakarta, Indonesia.
IDENTIFYING SOCIOECONOMIC, PSYCHIATRIC, AND BIOLOGICAL RISK FACTORS IN PSYCHOGENIC NONEPILEPTIC SEIZURES

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¹Hawaii Pacific Neuroscience, Clinical Research Center, Honolulu, United States of America, ²University of Hawai‘i at Mānoa, John A. Burns School Of Medicine, Honolulu, United States of America

Background and Aims:: PNES make up 20-30% of diagnoses for intractable epilepsy, resulting in incorrect treatment and unnecessary medical cost. The aim of this case-control study is to identify risk factors associated with the development of PNES, which could potentially aid with earlier disease recognition.

Methods:: To identify socioeconomic and medical risk factors unique to PNES, a retrospective case-control study was conducted at an epilepsy center in Hawaii. After excluding patients without a video EEG, 101 patients were identified. Two sets of randomly-selected controls were utilized: 303 unmatched and 202 matched by age, sex, and race.

Results:: PNES median age was 43 (IQR 30-54), 16 years younger than controls (95%CI:12.00-21.00), p=7.95x10⁻¹². Median household income was $3760 (95%CI:0.00029-10935;p=0.0054) less amongst PNES patients.

Table 1: Socioeconomic and psychiatric variables in PNES vs. Matched controls

<table>
<thead>
<tr>
<th>Factor</th>
<th>Odds Ratio</th>
<th>Confidence Interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Private Insurance</td>
<td>0.52</td>
<td>0.32-0.84</td>
<td>0.012</td>
</tr>
<tr>
<td>Medicaid</td>
<td>1.75</td>
<td>1.04-2.94</td>
<td>0.043</td>
</tr>
<tr>
<td>Homelessness</td>
<td>10.39</td>
<td>1.14-496.23</td>
<td>0.012</td>
</tr>
<tr>
<td>Drug Use</td>
<td>3.47</td>
<td>1.84-6.64</td>
<td>0.00012</td>
</tr>
<tr>
<td>Anxiety</td>
<td>5.41</td>
<td>3.18-9.35</td>
<td>2.5 x 10⁻¹⁰</td>
</tr>
<tr>
<td>Depression</td>
<td>3.10</td>
<td>1.80-5.28</td>
<td>8.6 x 10⁻⁶</td>
</tr>
<tr>
<td>PTSD</td>
<td>7.26</td>
<td>2.83-21.04</td>
<td>2.6 x 10⁻⁶</td>
</tr>
<tr>
<td>Bipolar Disorder</td>
<td>3.57</td>
<td>1.14-12.35</td>
<td>0.023</td>
</tr>
<tr>
<td>Traumatic History</td>
<td>32.52</td>
<td>7.80-287.5</td>
<td>2.4x10⁻¹¹</td>
</tr>
</tbody>
</table>

Table 2: Variables by race within PNES

<table>
<thead>
<tr>
<th>Factor</th>
<th>White (OR (95% Confidence Interval))</th>
<th>NHPI (OR (95% Confidence Interval))</th>
<th>Asian (OR (95% Confidence Interval))</th>
<th>Other (OR (95% Confidence Interval))</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNES¹</td>
<td>0.97(0.59-1.58), p=1.0</td>
<td>2.12(1.26-3.54), p=0.0032</td>
<td>0.43(0.22-0.81), p=0.0082</td>
<td>0.89(0.36-2.01), p=0.92</td>
</tr>
<tr>
<td>Depression</td>
<td>0.56(0.23-1.37), p=0.23</td>
<td>2.51(1.00-6.64), p=0.052</td>
<td>0.22(0.05-0.82), p=0.012</td>
<td>6.62(0.83-304.70), p=0.074</td>
</tr>
<tr>
<td>PTSD</td>
<td>0.57(0.16-1.77), p=0.33</td>
<td>3.53(1.18-11.18), p=0.02</td>
<td>0.07(0.00-0.42), p=0.032</td>
<td>1.10(0.01-6.42), p=1</td>
</tr>
<tr>
<td>Drug Use</td>
<td>0.68(0.24-1.84), p=0.55</td>
<td>3.05(1.11-8.61), p=0.027</td>
<td>0.05(0.00-0.28), p=0.0093</td>
<td>2.25 (0.41-11.42), p=0.26</td>
</tr>
</tbody>
</table>

¹Compared to unmatched controls
Conclusions: There are socioeconomic and racial disparities that play a role in the development of PNES.
FXTAS SYNDROME: NEUROPSYCHIATRIC FEATURES

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Background and Aims:: Le syndrome de tremblement et d'ataxie associé à l’X fragile (FXTAS) est une maladie neurodégénérative développé par des porteurs d’une prémutation dans le gène fragile X mental retardation 1 (FMR1). To study the neuropsychiatric profile and paraclinical features of FXTAS patients.

Methods:: All patients underwent a neuropsychological assessment, brain MRI and an ENMG study.

Results:: We included 3 patients with sex-ratio 0.5. Cerebellar ataxia was the initial manifestation in all patients with an onset age of 50 years. Pyramidal signs and peripheral neuropathy were present in two patients respectively. Mean MMSE was 26/30 with executive function deficits, anxiety and depression in all patients. Brain MRI showed bilateral hyperintensities of the middle cerebellar peduncles (MCP sign) on FLAIR images in all patients.

Conclusions:: FXTAS has a high penetrance in males and variable penetrance in females in accordance with their X-inactivation ratio. It usually manifests in the early 60s, typically beginning with intention tremor followed by cerebellar ataxia. However, up to 20% of FXTAS patients can develop ataxia without concomitant tremor like in our patients. Cognitive deficits include executive and/or attentional dysfunction. Behavioural features associated with the premutation alleles include anxiety, obsessive–compulsive traits and depression. They usually worsen with cognitive decline. MCP sign is the hallmark of FXTAS correlating with motor symptoms as well as cognitive and behavioural features. FMR1 premutations are associated with a variety of manifestations and phenotypes. Neuropsychiatric problems are quite common in carriers and usually present early in life, which could be problematic and requiring medical treatment.
PSYCHOSIS AS AN UNUSUAL BEGIN OF CREUTZFELDT – JAKOB

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Background and Aims:: Creutzfeldt-Jakob disease (CJD) is an extremely rare and devastating disease characterized by rapid neurological deterioration in a healthy individual. The classic clinical presentation of CJD includes rapidly progressive dementia, myoclonus, pyramidal, extrapyramidal and cerebellar signs. Although it is less frequent that the disease begin with non-specific psychiatric signs.

Methods:: Retrospective study of a patient diagnosed with CJD

Results:: We reported the case of a 66-year-old woman without personal or familial psychiatric history. Initial symptoms included delusions of persecution, depressed mood, memory loss, and a strange sensation. His sons stated that his cognitive problems had worsened significantly in the previous two weeks and associated with visual, auditory and sensory hallucinations. The physical examination was significant for perseverance, agnosia and apraxia associated with depressed mood and loss of vital momentum. His muscle tone was normal at all four extremities. Magnetic resonance imaging showed high signal intensity in the bilateral caudate, putamen and left frontotemporal cortex in T2-weighted and diffusion-weighted imaging. Studies on cerebrospinal fluid were also performed. The number of cells, glucose and proteins were within normal limits its 14-3-3 protein level was positive.

Conclusions:: Our patient was diagnosed with probable CJD, based on internationally-agreed diagnostic criteria. This fatal neurological disease occurs in sporadic, familial and acquired forms. Psychiatric symptoms are considered rare; in early stages of the disease they are found in up to 40% of the cases. However, presentation as a pure psychotic condition over so many months of development is not typical.
SNEEZING AS CONVERSION DISORDER: DIFFERENT FACES OF THE SAME FRAGILITY.

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Background and Aims:: Sneezing is a common symptom that can be caused by many factors such as foreign substances, allergies, chemical irritants and other less common factors. Intractable paroxysmal sneezing is a very rare condition and just a small number of cases have been reported. The majority of these studies are mainly referred to adolescent female patients and some children, in which intractable sneezing had psychogenic origins. Common clinical features of conversion disorders, like headache and pseudo-seizures, can rotate to time or manifest even in the same patient simultaneously. The aim is present a case of psychogenic intractable sneezing occurred in an adolescent patient.

Methods:: The sneezing, persisted for several consecutive days, used to be continuous whereas open eyes, except during sleep, with a frequency of once every 5-60 seconds. The patient had a past medical history of gastralgia and tachycardia during last 8 month and headache started when the girl was 12 years old. Although ordinary examinations showed a regular clinical state, psychogenic stressors were recognized so she started anxiolytic drugs and supportive counselling. A series of psychiatric conversations were needed to convert symptoms into verbal externalizations with a progressive improvement of headache and cessation of sneezing.

Results:: The case perfectly describes an intractable paroxysmal sneezing disorders. Psychological counselling was one of the most beneficial therapy, whereas the others showed conflicting results.

Conclusions:: Psychogenic intractable sneezing is a real and debilitating disease. When ordinary examinations and investigations showed a regular clinical state, psychogenic stressors must be explored to make the correct diagnosis.
INVESTIGATING THE GENDER DIFFERENCE AND PREVALENCE OF DEPRESSION AMONG PATIENTS WITH FIBROMYALGIA AT THE NPZR

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Background and Aims:: Chronic pain among patients with FM may cause feeling of hopelessness and depression. According to a current meta-analysis a lifetime depression frequency among people with FM was % 65 (J.S.Loge-Hagena, et al., 2019). Additionally, fibromyalgia is more common in women (% 4.2) than men (% 0.2) (Mas, Carmona, Valverde, Ribas, & Group, 2008). This study aimed to investigate the prevalence of depression in patients with FM treated at the Neuro-Psychiatric Center in Riem (NPZR).

Methods:: A total of 96 FM patients (19.8%, n=19 male and 80.2%, n=77 female) diagnosed with FM were selected from patient files between 2015 and 2021. Clinical interviews and the Beck Depression Inventory (BDI) had been conducted in FM patients to measure the level of depression.

Results:: The sample showed a significant gender difference with 80.2% female patients, 49% of participants were between 51 and 60 years old. The study sample showed a high prevalence of severe depression (85.4%). Tinnitus, and migraine were the most common comorbidities (both 12.5%). 57.3% of patients enrolled in 2015 still continue their treatment.

Conclusions:: The ongoing research is in line with previous studies: FM patients are mainly female and older than 50 and demonstrate high levels of depression and comorbidities such as Tinnitus and Migraine.
A ‘SHOULDER TAP’ TEST FOR FUNCTIONAL GAIT DISORDERS: A SIGN OF ABNORMAL ANTICIPATORY BEHAVIOUR

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Background and Aims:: Functional gait disorders (FGDs) involve gait abnormalities that are internally inconsistent and incongruent with other neurological disease. The clinical pull (or retropulsion) test is widely considered the gold standard in evaluating postural instability in patients with neurological gait disorders. Here, we describe the range of postural responses to the pull test in patients with functional gait disorders (FGDs) and explore the utility of the ‘shoulder tap test’ in these patients.

Methods:: Patients with a diagnosis of FGD were identified from movement disorders clinics at Ashford St Peter’s and St George’s University Hospitals NHS trusts. Reactions to being ‘tapped’ at the shoulders or pulled were retrospectively analysed using clinical records. For the shoulder tap test, patients were instructed that “on the count of three please try to keep upright if you are moved backwards” and that they were allowed to take as many steps as needed to avoid falling.

Results:: Thirty-one patients with FGDs in whom responses were documented to either shoulder tap, pull test, or both were included in the analysis. All patients in whom a shoulder tap was performed (n=25) had an abnormal response, including taking multiple steps (n=9), significant body sway or a startle response (n=4), falling into the examiner’s arms (n=7), or anticipatory body movement before being tapped (n=4). Abnormal responses to pull were documented in 14/17 patients (82.35%).

Conclusions:: The ‘shoulder tap test’ was abnormal in all patients with FGD, even in those with a normal pull test, and may reflect postural hypervigilance and abnormal expectation in these individuals.
IMPACT OF COVID-19 PANDEMIC ON THE ACUTE CONFUSIONAL SYNDROME BY THE LIAISON PSYCHIATRY SERVICE OF HOSPITAL DEL MAR

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Background and Aims:: Introduction: Coronavirus Disease 19 (COVID-19) pandemic has had a profound worldwide impact on health. Since the outbreak the most common neuropsychiatric complication has been Acute Confusional Syndrome (ACS). Aim: To describe characteristics of the admitted patients attended by the liaison psychiatry service for ACS during the COVID 19 pandemic. Clinical and sociodemographic variables were described.

Methods:: Material and Methods: We conducted an observational, descriptive study. All patients attended by the liaison psychiatry service of Hospital del Mar, between February and April 2020, with ACS diagnosis were included. Results are described in terms of mean, standard deviation and proportion, depending on each variable.

Results:: We included 62 patients with acute confusional syndrome; 35 were men (56.5%), with a mean age of 71.71 years (standard deviation [SD]:11.3). The mean stay of hospital admission was 41.19 days [SD: 38.039]. The mean number of consultations carried out was 6.5 [SD: 5.422]. Half of our sample (52.5%) had confusional symptoms for 8 days. 50 patients presented complications during admission (80.6%), of which 43 patients developed infectious complications (69.4%). Almost the entire sample (59 patients) had a history of chronic diseases (95.2%). 54 patients (88.5%) had potential risk factors associated with acute confusional syndrome including: active infection in 46 (74.2%), hypoxemia in 25 (40.3%), isolation in 24 (39.3%) and previous cognitive impairment in 15 (24.6%).

Conclusions:: During the first pandemic crisis of COVID-19 confusional patients had many complications and many risk factors associated such as active infection, hypoxemia and isolation (which in turn are symptoms of COVID-19).
HIGH BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) AND NEGATIVE PSYCHOLOGICAL FLEXIBILITY AS POTENTIAL PREDICTORS OF EARLY FATIGUE SYNDROME IN HEALTHY FEMALES.

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Background and Aims: Fatigue is one of the most common non-specific symptoms complaints in an apparently healthy person. Recent studies showed that enhancing psychological flexibility could improve fatigue interference. Our study aims to explore the association of fatigue with psychological flexibility and related biomarkers.

Methods: A cross-sectional study gathered data from a baseline characteristic mindful volunteer. Each participant was self-evaluated with the questionnaire of fatigue and psychological flexibility. They have also been evaluated by potential factors causing fatigue as sleep quality by the Pittsburgh sleep questionnaire and self-evaluated sleep quality, depression by PHQ-9. The participants were evaluated potential biomarkers related to psychological flexibility including HRV, serum cortisol, and BDNF within one week after responding to the questionnaire.

Results: The evaluation was done on 47 healthy females including 22 nurses and 25 occupational therapy students, mean age 29.70 ± 12.55 years. The prevalence of fatigue is 38.30%. The bivariate analysis comparing fatigue and the non-fatigued group showed higher negative psychological flexibility score (15.44 ± 5.81 vs 9.14 ± 4.19, p=0.001), higher PSQI score (8.39 ± 2.95 vs 5.97 ± 2.67, p=0.006) and higher BDNF (7.60 ± 3.46 vs 5.69 ± 3.74, p = 0.04) in the fatigue group. The multivariate analysis showed the independent factors associated with fatigue including negative psychological flexibility (OR 1.31, p=0.03) and high BDNF (OR 1.33, p=0.05).

Conclusions: Our study supported the previous finding that psychological flexibility was an independent association with fatigue. BDNF showed association with fatigue which may be the potential biomarkers for detecting early fatigue conditions.
THE LANGUAGE OF SCIENTIFIC VALIDATION IN TRANSLATIONAL NEUROSCIENCE: FROM THE HERMENEUTICS OF THE SYMPTOM TOWARDS A CONTINUUM PARADIGM

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Background and Aims:: The current challenge in the biological study of Neuropsychiatry - particularly, in Major Depressive Disorder - consists of avoiding exercising a reductionism in the language of psychopathology by naturalizing its symptomatology (Berrios, 2011). For this, it is essential to observe the conceptual aspects inherent to the validation of the methods applied in their study. However, it is paradoxical to recognize that, in numerous neurobiological research projects, this observation is hardly considered relevant due, fundamentally, to the heterogeneous conceptual evolution that experimental validation criteria present. The general objective of this work is to develop a study with logical and chronological rigor of the conceptual evolution of the validation criteria applied to experimental models in the basic research of Depression.

Methods:: A posteriori, this task will involve a pertinent bibliographic review, in order to rethink the meaning of scientific understanding from the creative power of words (Lacan, 2017).

Results:: The language of psychopathology is based on the implications that the subject's discourse manifests in the organization of their own psychic body, because their unconscious has the structure of a language (Lacan, 2017). Consequently, basic research of Depression requires a translational continuum approach (Belzung, Lemoine, 2011) that allows to revalue the hermeneutical dimension of the symptom.

Conclusions:: Finally, the notion of scientific understanding is inherent to the conceptual validation of the investigation methodology (Geyer, Markou, 1995), as it is in words where reside the concepts that constitute the time of the phenomena (Lacan, 2017) which will be known by virtue of their symbolic nature.
WORKPLACE VIOLENCE AGAINST DOCTORS IN KHARTOUM STATE, SUDAN 2020

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Background and Aims:: Workplace violence against health care workers and especially doctors are now clearly taken as a rapidly rising health problem in Sudan with great political and legal issues concerns. This study aimed to explore the prevalence of verbal and physical workplace violence, the major factors associated with it, and its consequences reported by medical staff at Khartoum, Sudan governmental hospitals 2020.

Methods:: This is a cross-sectional survey. Self-administered questionnaires were used to collect data on aspects of workplace violence against doctors in Khartoum, Sudan governmental hospitals. An online questionnaire were distributed randomly in online doctor's groups. The data were analysed by SPSS version 26.

Results:: About 195 (50%) participants experienced one type of violence, either physical or non-physical. The assailants were mostly males in the age group of 19-35 years (70.2%), most of them were under no influence (60.8%). The most frequent consequence of violence was anger and the majority treat themselves, 79.1% of the respondents did not report the incident mostly because it was useless and from their experience, no action would be taken.

Conclusions:: Approximately one in every two doctors has experienced some degree of violence either physical or non-physical violence or both, and it was negatively reflected on their psychological status as well as their work performance.
A SYSTEMATIC REVIEW OF OVERLAPPING AFFECTED BRAIN AREAS IN SEVERE MENTAL DISORDERS ADULT INPATIENTS

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Background and Aims:: In severe presentations, major depressive disorder (MDD), schizophrenia (SZ), and bipolar disorder (BD) can be categorized as severe mental disorders (SMD). Despite the clinical attributes that outline them, studies have demonstrated overlapping genetic, biological, and environmental aspects, including neuroimaging findings. Our aim is to evaluate structural magnetic resonance imaging and computed tomography findings in adult inpatients diagnosed with SMD and hospitalized at psychiatric wards.

Methods:: PubMed, Embase, PsycInfo, Cochrane Library, and Web of Science were searched up to May 27th, 2021, using predefined terms and criteria. Articles were screened and extracted by two independent groups, with third-party raters for discrepancies. Quality of evidence was evaluated with the Newcastle-Ottawa Scale. Synthesis was made by qualitative analysis. This study is registered on PROSPERO (CRD42020171718) and followed the PRISMA protocol.

Results:: 35 studies were included, of which none was considered to likely introduce bias in our analyses. Overlapping areas in MDD, SZ, and Affective Psychosis (AP) patients, which include BD and MDD with psychotic features, are presented in the inferior temporal and cingulate gyri. MDD and SZ disorders had commonly affected areas in the inferior and middle frontal gyri, transverse temporal gyrus, insula, and hippocampus. Considering the analyses of SZ and AP, commonly affected areas were found in the temporal pole.

Conclusions:: Overlapping affected areas among SMD patients are reported, but the heterogeneity of studies’ designs and findings are still a limitation for clinically relevant guidelines. New neuroimaging resources and longer longitudinal designs with bigger samples are necessary to enable reliable pathophysiological data of SMD patients.
Background and Aims: Impaired social cognition is frequent in individuals with schizophrenia (IS); however, how far predicting the intentions of others is affected is unclear. We have previously shown that healthy individuals can predict social intentions and adapt their behaviour, whereas individuals with prediction deficits, like autism spectrum disorder, fail to do so. This study aims to assess prediction deficits in IS using a novel neuropsychological method.

Methods: We included 9 IS and 4 healthy controls (adults). All participants played a game where they interacted with a virtual agent while intercepting a target that moved downwards on the screen at different x-offsets. The agent displayed three different behaviours, neutral, invasive, or passive, which are representative of social intentions. To analyse this interaction, we extracted psychometric curves based on the subject’s responses and obtained the point at which the subjects displayed a 50% probability to move towards the target (Fig. 1 and 2). Its shift from the centre indicates the bias induced by the agent's behaviour.
**Results:** Our preliminary results show that both groups adapted to the agent’s behaviour. However, only IS displayed a significant difference in a shift from the neutral behaviour and a close to significant difference in the invasive behaviour compared to the control group (Fig. 3).

**Conclusions:** By analysing the responses to social behaviours we assessed whether IS present prediction deficits. The results demonstrated a tendency for IS to react differently to “invasive behaviour” compared to controls. This resonates with the notion that IS might attribute intentions differently than healthy individuals.
ANALYSIS OF POPULATION DISTRIBUTION OF GENOTYPES RELATED TO METABOLIC SYNDROME INDUCED BY ANTIPSYCHOTIC DRUGS

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Background and Aims: To explore the relationship between different genotypes of antipsychotic drugs and metabolic syndrome, and to analyze the distribution characteristics of population in western China.

Methods: To collect a 3 armour hospital patients with mental disorders caused by drug metabolic abnormalities, a total of 202 cases, the application of self-made questionnaire survey general demographic data, height, weight, duration, hospitalization time, drug usage, etc., according to the course, use according to the Chinese medical association suggested that suitable for China's syndrome diagnostic criteria identified patients with MS. Data statistical analysis software was used to summarize and analyze different genotypes.

Results: 1. There were differences between the C/C, -/C, -/ - genotypes of HTR1ARS6295 and the therapeutic effect of antipsychotic drugs on patients with metabolic syndrome. 2. People with metabolic syndrome caused by antipsychotics had a worse response rate than those with genetically guided mental disorders, with an overall response rate reduced by 23.85%. 3. Metabolic syndromes induced by antipsychotics appeared to be undifferentiated across all genotypes, but polymorphisms of DRD3rs6280, HTR2ARS6513, and MC4RRS17782313 were different from metabolic syndromes induced by antipsychotics. C/T gene mutation in DRD3RS628, A/A gene mutation in MC4RRS1772313, and T/T gene mutation in HTR2ARS6513 are more likely to produce metabolic syndrome under antipsychotic treatment. 4. The number of cases of metabolic syndrome screened out in this study was small, so the number of patients with different genotypes was small or 0, which affected the overall judgment.

Conclusions: DRD3rs6280, HTR2ARS6513 and MC4RRS17782313 were found with metabolic syndrome.
PET-MRI FINDINGS IN IDIOPATHIC INFLAMMATORY MYOSITIS: A FIRST STUDY

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Background and Aims:: We sought to determine the utility of PET-MRI in diagnosing Idiopathic Inflammatory Myositis (IIM), and look for correlation between FDG uptake and clinical, pathological and laboratory parameters.

Methods:: A retrospective, observational study was conducted on twenty-two patients of IIM, having positive serum autoantibodies, who underwent PET-MRI (3-Tesla SIEMENS Biograph MR scanner) from 2017-2020. Thirty patients who underwent PET-MRI for detection of systemic metastasis, without muscle involvement formed the control group.

Results:: In the IIM cohort, Female:Male ratio- 1.44, mean age at diagnosis- 42.23 ± 12.02 years, and the mean duration of illness- 8 ± 6.4 months. 72.73% patients had moderate to severe, predominantly proximal limb weakness. Serum autoantibodies identified were Mi2B(40.9%), PL-7(9.1%), PL-12(9.1%), SRP(13.64%), Ro-52(36.36%), PM-Scl, U1-RNP, ANA(27.27%). Whole body PET-MRI showed a sensitivity of 100% with 86.7% specificity in diagnosing IIM, using SUVmean Ratio to quantify FDG uptake. FDG uptake was maximum in pelvic girdle followed by pectoral girdles. Multivariate regression analysis showed severity of muscle weakness, MiB2A antibody positivity and creatinine kinase levels had significant positive correlation with FDG uptake in PET-MRI (P value- 0.002, 0.014, 0.032 respectively for limb FDG uptake). FDG uptake also showed good correlation with histopathological features (severity of muscle inflammation, interstitial edema) and muscle MRI (muscle edema in T2-STIR), but there was no significant association with treatment response.
Conclusions:: Current study confirms that PET-MRI is a promising diagnostic modality for IIM and it reflects the severity of myositis. Further it can identify malignancy as small as 7mm. One patient with Dermatomyositis had carcinoma ovary in our cohort.
Background and Aims:: The coronavirus disease 2019 (COVID-19) pandemic has severe implications for individuals' health, daily activities, and economy worldwide. We launched a web-based questionnaire survey on May 11, 2020, to clarify the impact of COVID-19 on patients with muscular dystrophy.

Methods:: We inquired about impacts on medical care, home/facility services, daily life, support, health conditions, and infection with severe acute respiratory syndrome coronavirus 2.

Results:: By the end of February 2021, 663 participants completed the survey. Approximately 28% of patients postponed regular consultations, and 23% of patients who underwent consultations more than once a month used telephone consultations. Two of 97 patients with Duchenne muscular dystrophy taking steroids had reduced their doses. A shortage of ventilator accessories and infection protection equipment occurred following the onset of COVID-19, and this shortage had a significant impact on medical care and infection prevention measures. The lives of most school-aged patients were affected because of school closures and remote learning. More than 20% of patients reported physical or mental complaints. Some patients with mild disease complained of deteriorating motor performance due to decreased rehabilitation and the avoidance of going out. Some patients with advanced-stage disease complained of an increased care burden due to reduced service use and mental stress due to information flooding and restrictions in visiting family or friends. Two patients contracted and recovered from COVID-19.

Conclusions:: COVID-19 has significantly affected the activities and quality of life of patients with muscular dystrophy. We will continue this survey and analyze the longitudinal changes.
ACUTE HYPOKALIEMIC MYOPATHY DUE TO CHRONIC LICORICE INGESTION: A CASE REPORT.

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Background and Aims:: Glycyrrhetinic acid, a steroid-like glycoside contained in licorice, has a mineralocorticoid activity by inhibiting the enzyme that transforms cortisol into cortisone (11β-HSD2) resulting in overactivity of mineralocorticoid receptors. This pseudohyperaldosteronism condition may result in a severe hypokalemia and impairment of muscle lipid metabolism with rhabdomyolysis.

Methods:: We report the case of a 57-year-old woman who developed subacute proximal symmetrical flaccid tetraparesis associated with generalized muscle pain, peripheral paresthesias and areflexia.

Results:: EMG showed spontaneous activity with recruitment of small amplitude, short duration and polyphasic motor units and interference facilitation (myopathic pattern with necrosis signs). Blood examinations were suggestive of rhabdomyolysis (iperCPKemia and increase of other cytolisis indexes), with severe hypokaliemia (1.7 mmol/L), metabolic alkalosis, low serum aldosterone concentration and plasma renin level. ECG showed sagging of the S-T segment, depression of T wave and elevation of U wave. Repeated careful history-taking revealed chronic daily ingesting of tablets of pure licorice and licorice-containing herbal teas for years. The intake was stopped and the patient was treated with organic potassium salts by intravenous and oral route, with complete recovery and normalization of laboratory parameters in a few weeks.
Conclusions: Mineralocorticoid activity of licorice is well-known but severe acute hypokaliemic myopathy due to chronic ingestion has rarely been reported. Clinical severity may depend on daily dosage, duration of use and different individual susceptibility. We suggest that this clinical entity, often underdiagnosed, should be considered in the differential diagnosis of acute flaccid tetraparesis with hypokaliemia to avoid life-threatening diagnostic and therapeutic delay.
A PATIENT WITH NEUTRAL LIPID STORAGE DISEASE WITH MYOPATHY (NLSD-M): A CLINICAL AND GENETIC STUDY

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Background and Aims:: Neutral lipid storage disease with myopathy (NLSD-M) is an autosomal recessive disorder characterized by triglyceride-containing cytoplasmic droplets in leukocytes and muscle tissue. Usually, it presents with adult onset slowly progressive proximal muscle weakness associated with hypertrophic cardiomyopathy.

Methods:: We studied a 42-year-old patient presenting with progressive proximal upper limb weakness since age 38. Clinical examination showed both asymmetrical (right>left) proximal upper limb weakness and difficulty in walking on heels. Mild weakness of both orbicularis oculi muscles was also observed.

Results:: Diffuse cytoplasmatic accumulation of lipid droplets was detected on muscle biopsy and Jordan anomaly, a well-known NLSD marker, was found by peripheral blood smear. Genetic analysis displayed a novel homozygote deletion in the PNPLA2 gene (exon2: c[45_47del]) causing the [Gly16Del]. Both unaffected parents harbored the heterozygote deletion. Upper-limb muscle MRI showed atrophy of the supraspinatus and infraspinatus muscles, especially on the right side. Cardiac focal inferolateral intramural fibrosis was noted by MRI as a possible manifestation of lipid accumulation. However, no cardiac involvement was clinically detected.

Conclusions:: Our study suggests that 1) distal muscle involvement can be present in NLSD-M, 2) in Italian patients cardiac involvement is usually mild, differently from Far East subjects in which it is frequent and often leads to heart transplantation, 3) infraspinatus muscle is one of the most radiologically affected muscles and 4) Italian families usually harbor private mutations. Moreover, our patient presents with orbicularis oculi muscle weakness, indicating that facial muscles can also be involved and confirming clinical heterogeneity of this disease.
Background and Aims:: Colchicine is derived from the corms of Colchicum autumnale. The drug has been used therapeutically for more than 200 years in the treatment of various diseases such as Gout, Familial Mediterranean Fever (FMF), and Behcet’s disease; yet, its myotoxicity adverse reaction has not only been documented before 1996 in the British National Formulary. Colchicine induced myopathy has been described in patients with chronic renal failure and patients who are using a concomitant drug like a statin. However, pure myopathy caused by Colchicine never been reported from Saudi Arabia.

Methods:: Case Report and literature review.

Results:: This report describes a 64-year-old patient who presented with upper and lower limb weakness after two weeks of taking Colchicine for his recently diagnosed gout arthritis. He had a proximal weakness, and his muscle enzymes were very high. Furthermore, the needle electromyographic examination (EMG) demonstrated abundant fibrillations, myotonic discharges, and myopathic motor units. Two weeks after colchicine cessation, his weakness improved dramatically with normalization of CK and disappearance of myotonic discharges in the repeated EMG.

Conclusions:: This report presents the first case in Saudi Arabia that demonstrates the typical clinical presentation of Colchicine induced myopathy. Colchicine-induced myopathy is an infrequent toxic complication. Therefore, clinicians should be aware of this rare side effect, as clinical suspicion is the most important diagnostic clue, and the only effective treatment is the termination of the Colchicine.
MUTATIONAL SPECTRUM OF DYSFERLINOPATHIES IN A LARGE INDIAN COHORT

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Background and Aims:: One hundred and twenty three patients clinically diagnosed with dysferlinopathy underwent genetic analysis to identify the spectrum of mutations in a Large Indian cohort

Methods:: Next generation sequencing was used for genetic testing

Results:: Median age at onset=21 years(2-50 years, Q1-17,Q3-25), median duration illness=48 months (3 - 288 months, Q1-24, Q3-72). M:F=2.2:1. Among these pathogenic/ likely pathogenic were:101 homozygous, 11 compound heterozygous variations in DYSF.Further, from remaining 11 cases[1 had compound heterozygous with one pathogenic mutation and one VUS, 1 carried compound heterozygous with one pathogenic and benign variant, 2 had homozygous VUS and 7 had single heterozygous variant with 5 being pathogenic/ likely pathogenic and 2 VUS. Three had additional variations in other genes-CHRNE (Homozygous, Pathogenic), CAPN3 (Heterozygous, likely pathogenic,) LAMA2 (Heterozygous, VUS,). From sample of 123, 84 variants were identified in DYSF, including, 76 pathogenic/likely pathogenic, 6 VUS and 2 benign, according to ACMG classification. Thirty nine novel variants identified, (36 pathogenic/likely pathogenic and 3 VUS) and 45 known variants (40 pathogenic/likely pathogenic, 3 VUS and 2 benign). Among 76 pathogenic/likely pathogenic variants, 21 were missense (9 novel), 17 frameshift (12 novel), 12 nonsense (4 novel), 4 in-frame deletion (2 novel) and 2 exonic deletion (both novel) mutations. Five pathogenic variations were in exon 29 , and p.Arg1064His was most recurrent mutation (13 homozygous and 2 compound heterozygous).

Conclusions:: We describe the spectrum of mutations and the most recurring mutation in a large single center cohort of Indian population suspected to have Dysferlinopathy.
MAGNETIC RESONANCE IMAGING OF MUSCLES IN ANTI-MI2B INFLAMMATORY MYOSITIS AND CORRELATION WITH CLINICAL FINDINGS

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Background and Aims:: We sought to determine Magnetic resonance imaging (MRI) characteristics of muscles in Anti-Mi2b Inflammatory Myositis, and look for correlation between imaging findings with clinical parameters.

Methods:: A retrospective, observational study of sixteen patients of anti-Mi2b positive inflammatory myositis, who underwent lower limb MRI-axial STIR, T1 sequences (1.5 T Aera ; SIEMENS healthcare MR scanner) from 2017-2020. Manual Muscle Testing-8 (MMT 8) was used for clinical severity, modified Stramare scoring to grade muscle edema and modified Mercuri scale for muscle atrophy on MRI.

Results:: In this cohort, F:M=1, median age at diagnosis 46.5 years (Q1=34.25,Q3=54.25), median duration of illness 10 months (Q1=3,Q3=34.5). The most severely affected muscles were vastus intermedius, vastus lateralis followed by iliacus, iliopsoas. Gluteus medius and minimus muscle edema showed significant correlation with Creatine kinase(CK), however, there was no significant correlation between muscle edema of most muscles and MMT-8, CK. MMT-8 did not correlate with CK values by Spearman ’s rho test. There was a trend towards correlation of muscle edema in rectus femoris, semitendinosus and soleus with CK. None of the muscles had atrophy of grade > 3. All showed fascial edema in thigh muscles.

Conclusions:: This study showed preferential severe affection of Hip and thigh muscles, however most of these muscles on Stramare scoring did not show significant correlation with MMT. Gluteal muscles showed correlation with CK. Fascial edema was uniform. we are planning to do larger study to conclude these findings.
Background and Aims: Myotonic dystrophy (DM1) is a multisystem disease that involves several organs including brain and muscles. Foot drop, gait alteration, and high risk of falling are core features of the disease. Rehabilitative approaches may benefit from a deeper understanding of how foot drop impairs gait. This pilot study aims to evaluate foot drop by merging clinical and kinematic analysis.

Methods: A cohort of 39 patients with genetically confirmed DM1 and able to walk without any support was evaluated. Quantitative muscle test and six-minute walk test (6MWT) were performed. In addition, 13 patients and 11 healthy controls (HC) underwent the 10-meter Walk Test while wearing kinematic sensors at the legs. An amplitude analysis (AR) and a power spectral density analysis (PR) of the ankle angles during gait were performed, conducting to a severity index (Norm2). Descriptive statistics, t-test, and correlation test were analyzed.

Results: A direct correlation was found between foot dorsiflexors strength (FDS) and 6MWT ($p<0.01$) in the DM1 cohort. The kinematic analysis differentiates well DM1 from HC. AR, PR, and Norm2 showed a good inverse correlation with FDS ($r = -0.86$ $p<0.001$).

Conclusions: Foot drop is a core feature of DM1 and exposes patients to reduced mobility and a greater risk of falling. Dorsiflexors strength loss correlates with a poorer performance at functional outcomes such as 6MWT. The kinematic analysis may improve patients’ stratification based on strength loss and functional capacity. These findings further clarify how foot drop affects gait and help to create a tailored rehabilitation program for each DM1 patient.
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Background and Aims:: Sarcoglycanopathies are autosomal recessive forms of Limb-girdle muscular dystrophies (LGMD) caused by mutations in SGCA, SGCB, SGCG, and SGCD. The genetic architecture of sarcoglycanopathies in Indian patients is inadequate. In the present study, we aimed to investigate the clinical manifestations and the genetic basis of patients who are suspicious of being affected by sarcoglycanopathies.

Methods:: Detailed Clinical examination and lab investigations were done. NGS was performed in probands and family members with suspected LGMD.

Results:: A total of 37 different variants were detected in sarcoglycan genes in 72 cases (39 male, 33 female, age 5-50 years). 46 probands have consanguineous parentage. Thirty-one variations were predicted to be pathogenic /likely pathogenic, 24 (77%) are known, 7 (23%) are novel. These confirmed the clinical diagnosis in a total of 63 (88.73%) probands with biallelic variations [SGCA-18; SGCB-33; SGCG-7; SGCD-5], a single heterozygous variant in one patient. The most common mutation was c.544A>C (p.Thr182Pro) in SGCB, which was detected in 20 patients (27.77%). The majority of pathogenic mutations were homozygous (n=29; 96.6%), while compound heterozygous and single heterozygous mutations were once each. Variants in 7 cases were of uncertain significance (5 cases) and benign (2 cases) nature. 16 patients (six harbors c.544A>C (p.Thr182Pro) in SGCB) have loss of ambulation at the mean age of 14.1±9.1 years, after about 8.7±7.3 years into the illness. Only 2 patients had cardiac symptoms and one had respiratory system involvement.

Conclusions:: Our study suggests mutations in SGCB are the most common, followed by SGCA, SGCG, and SGCD, expanding the mutational spectrum. This is the first study with a large cohort of genetically confirmed sarcoglycanopathy patients in India.
PHENOTYPE GENOTYPE CHARACTERIZATION OF FKRP MUTATIONS IN AN INDIAN COHORT OF LIMB GIRDLE MUSCULAR DYSTROPHY

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**Background and Aims:** Mutations in the FKRP (Fukutin Related Protein) gene produces variable phenotypes including Limb Girdle Muscular Dystrophy Type R9 (formerly LGMD2I). It has been rarely reported in South Asian population. We studied a cohort of Indian patients with LGMD2I to elucidate the mutation spectrum and possible genotype–phenotype correlation.

**Methods:** Next-Generation Sequencing was performed in probands and family members with suspected LGMD.

**Results:** A total of eight patients (M: F = 4:4) were genetically diagnosed to have FKRP-R-CMD. The median age of onset was 30 months and age at presentation was 5 years (range 1.5-17 years). Putative disease-causing SNPs identified were as follows: hom. c.1343C>T/p.P448L (n=2), hom. c.646C>T/p.R216W (n=1), hom. c.160C>T/p.R54T (n=1), het. c.1060_1061inv/p.G354P (n=1), hom. c.650C>A/p.P217Q (n=1), het. c.942_943insC/p.C317Lfs*73 (n=1), het. c.933_934del/R312Lfs*77 (n=1) in exon 4 of the FKRP gene. Of these c.1343C>T and c.160C>T are previously reported and others are novel SNPs. Three subjects with heterozygous SNP are included as the clinical phenotype and histological findings strongly suggest features of FKRP related dystroglycanopathy. Delayed milestones, progressive proximal weakness was noted in 5 (62.5%), limb girdle phenotype was seen in 3/8 (37.5%), calf pseudohypertrophy was seen in 6/8 (75%), and consanguinity was present in 3/8 (37.5%) patients. Creatinine kinase was markedly elevated in all with a median of 8519.5 U/L (24-229 U/L). Cardiomyopathy was noted in one patient (12.5%).

**Conclusions:** The novel variations identified in this study expands the mutational spectrum of LGMDR9. As of now, this is the first study of genetically confirmed patients with LGMDR9 from India.
DIAGNOSIS OF ANXIETY AND DEPRESSION IN PATIENTS WITH MYASTHENIA GRAVIS

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Background and Aims:: Mood disorders are the most common comorbidity in patients with myasthenia gravis (MG). In particular, anxiety and depression are not often diagnosed and treated. The aim is a comprehensive assessment of anxiety and depression in MG patients, using newly validated Russian versions of international questionnaires.

Methods:: The study included 73 patients with MG and 230 control subjects. For fatigue, anxiety and depression evaluation were used Fatigue Severity Scale (FSS), Fatigue Impact Scale (FIS), Beck Depression Inventory (BDI), Spielberger–Khanin State Trait Anxiety Inventory (STAI).

Results:: The studied patient cohort revealed clinically significant fatigue (69.9 %), moderate to severe depression (20.5 %), a high level of personal (64.4 %) and situational anxiety (27.4 %). The average FSS score ≥4.0 was found in 84.1% of patients with depression and 45.8% of patients without depression (p = 0.002). The results of the FSS showed a stronger correlation with the somatic subscale BDI (r = 0.588, p <0.001) than with the cognitive-affective subscale BDI (r = 0.293, p = 0.02). In our study we found that the presence of depression in patients with MG significantly increase fatigue indicators.

Conclusions:: Depression may increase muscle weakness and fatigue in patients with myasthenia gravis, despite the absence of correlation between the severity of the disease and the psychosocial subscale FIS, but psychosocial fatigue is the strongest predictor for the development of depression. Symptoms of depression can mimic the symptoms of myasthenia gravis and remain underestimated. Clinicians should pay more attention to evaluation of psychological state in these patients.
LIMB-GIRDLE MUSCULAR DYSTROPHY D2 AND CYTOKINES: A LINK TO HTV1 RESISTANCE

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Background and Aims:: To detect plasma cytokines changes in trasportinopathy LGMD-D2, with mutation in TNPO3 gene, encoding for transportin-3 protein, a nuclear import receptor for serine/arginine-rich proteins determining HIV-1 immunity, by unknown mechanism(s).

Methods:: This Luminex study was done in 4 patients expressing two different mutations: an Italian-Spanish family, the others of Hungarian stock. Plasma from 4 LGMDD2 patients and 4 controls were measured in duplicate. The expression levels of TNFRSF8, IFN-beta, IL-1-alpha, MMP-1, MMP-10, uPAR, IFN-alpha, IFN-gamma, IL-1beta, MMP-8, MMP-12, CCL2 JE (MCP-1), CCL18 (MCP-2), CD163,GRO-beta, mip-2, IL-1 RI, S100A8, ICAM-1, CD106, CCL7, MCP-3, MARC, CCL20,MIP-3 alpha, GRO alpha, CXCL5,IL-8/CXCL8 and S100A9 were measured by Multiplex Luminex Assay using two custom-made plates (R&D Systems). Cytokines concentration was calculated through Bio-Plex 200 System software or by manual interpolation. Statistical analysis was performed with the nonparametric Mann–Whitney test using GraphPad Prism v9 software.

Results:: The expression levels of IFN-beta were reduced 25-fold (p<0.005) in LGMDD2 versus controls, while IFN-alpha increased 2.05-fold. The level of GRO-beta was increased 1.65-fold (p<0.05), in LGMDD2, GRO-alpha was slightly modified (0.9-fold reduction). TNFRSF8 and ICAM-1 were 1.58-fold and 2.15-fold(p<0.001) enhanced, respectively, in LGMDD2. The levels of S100A8 (p<0.001) and S100A9 (p<0.005) were reduced 6-fold and 25-fold respectively, expression of IL1RI was 2-fold reduced (p<0.05) in LGMDD2 versus controls. IL1b levels were similar, IL1a was 2.52-fold increased in patients, CXCL5 was 1.51-fold enhanced,CXCL8 was 1.7-fold reduced, but not significantly. CCL7 (p<0.01) was increased 3.44 fold, CCL2 (p<0.05) decreased 1.47 fold in patients.

Conclusions:: Despite the low number of samples, significant changes in several cytokines were observed.
LONGITUDINAL, QUANTITATIVE ASSESSMENT OF HAND MUSCLE STRENGTH DECAY IN MYOTONIC DYSTROPHY TYPE 1 (DM1)

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Background and Aims:: Hand muscle weakness is a core feature of DM1 and outcome measures assessing finger pinch and grip strength should be available for natural history and trial studies.

Methods:: We longitudinally evaluated self-assessed hand muscle strength with a hand-held dynamometer (HDD) in 115 consecutive DM1 patients of either gender. Three-finger pinch and handgrip strength were annually recorded in both hands with an up to six-year follow up. Descriptive statistics, t test and correlation were performed.

Results:: Within-case coefficient of variance (CV) was 7 ± 7 % (mean±SD) for pinch and 7.2 ± 6.8 % for handgrip. Median values of pinch and handgrip were markedly reduced at baseline for both male and female patients as compared to sex-matched normal values. Patients who showed abnormal baseline values of pinch (80%) and handgrip (98%) were evaluated for annual rate of progression. At follow-up, patients’ values for both measures were significantly (p< 0.01) decreased at each assessment compared to baseline. Mean annual loss rate was of 8.1±2.9 % for pinch and 7.2 ± 2.7% for handgrip.

Conclusions:: Our results show that three-point pinch grip and handgrip, measured by HHD, reliably detect the baseline condition and the longitudinal progression of hand muscle power loss in DM1. These measures, therefore, seem suitable for being used as clinical outcomes within the timeframe of short-term natural history studies and clinical trials in DM1.
BULBAR ONSET MYASTHENIA GRAVIS: DIAGNOSTIC CHALLENGES AND MISSED OPPORTUNITIES

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Background and Aims:: Myasthenia gravis (MG) is a frequently encountered neuromuscular junction (NMJ) disorder in clinical practice with a prevalence of 5 to 15 cases per 100,000 Ocular symptoms are the presenting sign of the disease in 50% to 75% of patients, bulbar plus ocular symptoms in 23.17% & Myasthenic patients presenting with isolated bulbar symptoms are mostly about 20.73% When a patient comes with acute bulbar symptoms especially with dysphonia, it will lead to diagnostic dilemma as there are good number of causes, apart from laryngeal myasthenia which is an uncommon aetiology, as stroke, demyelinating neurological diseases, toxicity, infection and other causes.

Methods:: This is a case series report of isolated bulbar onset myasthenia gravis which is rarely found, all presenting with dysphonia as an initial manifestation of bulbar myasthenia, we could reach the diagnosis of bulbar onset myasthenia gravis (serologically and/or electrophysiologically by EMG, NCV, repetitive supramaximal stimulation and single fiber EMG) and exclude other common causes of acute bulbar weakness.

Results:: SFEMG was the highest diagnostic test in our cases especially when done to the bulbar muscles, even when the RNS test was negative and the serology showed borderline results

Conclusions:: Considering MG as one of the potential differential diagnoses among cases of new onset or recurrent unexplained bulbar symptoms, is of high importance as it gives good recovery outcome and the patient become nearly normal after treatment.
CLINICAL AND GENETIC PROFILE OF DUCHENNE AND BECKER MUSCULAR DYSTROPHY PATIENTS IN THE FAR WEST OF ALGERIA

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Background and Aims:: Duchenne's (DMD) and Becker's (BMD) muscular dystrophy are the principal causes of myopathy in male children. It is linked to a mutation in the dystrophin gene and is inherited in an X-linked mode. The aims of our study are to describe the clinical and genetic phenotype of BMD and DMD patients in the far west of Algeria.

Methods:: Our study is prospective carried out in the neurology department of Tlemcen university hospital between January 2018 and December 2020. We collected the personal and family history, clinical and paraclinical data assays of muscular enzymes, ENMG). Analysis of the DMD gene was performed by the following techniques: MLPA and Next Generation Sequencing (NGS).

Results:: 32 patients had the clinical phenotype of dystrophinopathy including 19 patients with a mutation in the DMD gene. The median age of our patients was 10 years with a mean age of onset of 4 years and 9 months. Inbreeding was found in 79% of cases, 15.7% had similar cases in the family. 79% of the patients had a clinical DMD phenotype, 21% a clinical BMD phenotype. All of our patients had a high CPK level and myopathic involvement in ENMG. DMD was observed in 79% of cases and BMD in 21% of cases. The initial symptomatology of our patients was: 84% for motor disorders; 26% for pseudo-hypertrophy of the calves, 10% for delayed walking and 5% for Hyper CKemie. Deletions were observed in 84.2% of cases, duplications in 5.3% of cases and point mutations in the remaining 10.5% of cases.

Conclusions:: Our study is the first carried out on dystrophinopathies in the far west of Algeria. Although our sample is small, genetic study has shown the heterogeneity of dystrophinopathies in our region.
THE OMMAYA CATHETER AS A TREATMENT FOR PAIN AND CHEMOTHERAPY IN MENINGEAL CARCINOMATOSIS PATIENT

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Background and Aims:: Meningeal carcinomatosis consists of focal or multiple malignant metastases of extraneural solid tumors in the leptomeninges and subarachnoid space. It’s a rare complication and neurological symptoms include headache and nonspecific nerve palsy. The standard diagnosis is obtained by the presence of malignant cells in the cerebrospinal fluid cytology. The prognosis is poor, the treatment is limited and aims at palliating symptoms and stabilizing or partial improvement in neurological status.

Methods:: This study aims to report a case of treatment for pain and chemotherapy in meningeal carcinomatosis patients by Ommaya catheter use.

Results:: Man, 56 years old. Diagnosed 6 months before with intestinal adenocarcinoma, had been treated by surgery, chemotherapy, and radiotherapy. He showed severe pain syndrome, mainly headache, refractory to systemic opioid and non-opioid analgesic therapy. The cerebrospinal fluid cytology confirmed the diagnosis of carcinomatous meningitis. The patient was submitted to palliative treatment with an Ommaya catheter (OC) for intrathecal chemotherapy and opioid analgesic. The OC reservoir was placed under the scalp and attached to a catheter that ends in the lateral cerebral ventricle. Thus, medicines were injected directly into the intracerebroventricular space optimizing the treatment. The Brazilian public health care “Sistema Único de Saúde” (SUS) supported all treatments.

Conclusions:: The OC possibility a safe and effective therapy for the palliative treatment of refractory pain at-home care in meningeal carcinomatosis patients, despite this the OC is unusual in Brazil.
PALLIATIVE CARE FOR PATIENTS WITH DEMENTIA AND COVID-19: ANALYSES FROM A MAJOR REFERRAL HOSPITAL IN SOUTH AMERICA

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Background and Aims:: People with dementia are at higher risk of developing severe COVID-19 and worse virus-related outcomes. In addition, triage systems in pandemics have low sensitivity for the need of palliative care, not allowing appropriate end-of-life support to many patients. The aim of this study was to evaluate the palliative care offered to patients with dementia and COVID-19 in a major referral hospital in South America.

Methods:: Descriptive study of adult patients with COVID-19 from a major referral hospital in the city of São Paulo, Brazil. Dementia was screened searching medical records for ICD F02-03. Patients were screened for the need for palliative care through Supportive and Palliative Care Indicators Tool (SPICT). Data were analyzed using Microsoft Excel 2016.

Results:: The sample was composed of 21 (37.5%) males and 35 (62.5%) females with median [IQR] age of 81 [72-88] years. In addition, 24 (42.8%) were from the wards, 23 (41.1%) from the emergency room, and 9 (16.1%) from the ICU. Regarding SPICT criteria, 52 (92.9%) were at risk of deteriorating and dying. Of the patients who met SPICT criteria, 28 (53.8%) had access to palliative care during hospitalization. By the end of the study, 29 patients (51.8%) died and 27 (48.2%) were discharged. Of the patients who died (n=29), seven (24.1%) did not have access to palliative care.

Conclusions:: In our study, there was a high mortality rate between patients with dementia and COVID-19, although a considerable percentage of them did not have access to palliative care before dying.
Background and Aims:: During the COVID-19 pandemic, many patients with stroke face delayed access to acute care. Also, they delayed getting in chronic stroke-related problems or complication management due to avoiding hospital visits and decreasing the number of service healthcare providers and service units from adaptation to the pandemic. Therefore, relative poor prognosis cases are higher in some areas and some periods. The aim is to guide palliative healthcare teams to manage end-of-life care in stroke during the COVID-19 crisis.

Methods:: This study is a narrative review of palliative stroke care among the COVID-19 pandemic.

Results:: The National Institutes of Health Stroke Scale (NIHSS) is the essential tool for evaluation. The scores 20 or higher should access palliative care consultation early because high scores can predict poor outcomes in both the short and long term. The palliative care approach for stroke is multidisciplinary collaboration. The goal and core of palliative care will be set based on individual formal or informal advanced care plans. The intensive safety awareness for a rehabilitation program, follow-up plan, complication monitoring for healthcare teams, caregivers, family members, close contact persons, and the patient himself should be developed and appropriately improved.

Conclusions:: Active multidisciplinary teams cooperate with assisted telemedicine, and virtual evaluation by specialists play significant roles in palliative care among COVID-19 situations.
THE IMPACT OF COVID-19 PANDEMIC ON DISEASE SEVERITY AND QUALITY OF LIFE IN PARKINSON’S DISEASE

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Background and Aims:: Background and Aims-The challenges being faced during the lockdown period may worsen motor or non-motor symptoms in Parkinson’s disease (PD). This study was undertaken in order to investigate the impact of lockdown on the disease activity, caregiver perceptions and the quality of life of Parkinson’s disease patients.

Methods:: Materials and Methods-This cross-sectional study was conducted from June till September 2020. Sixty four PD patients and caregivers were interviewed telephonically after obtaining consent. The responses were recorded by means of a structured questionnaire. Non-motor symptoms scale (NMSS) and the Parkinson Disease Questionnaire-8 (PDQ-8) were applied. PDQ-8 severity index (PDQ-8 SI) scores were expressed as percentage of the raw PDQ-8 score out of the total score. SPSS 20.0 was used for statistical analysis.

Results:: Results-Out of 64 patients, 39 (60.9%) were males and 25 (39.1%) were females. The overall median age was 65 (55.25-69.75) years. The median duration was 48 (30-84) months. Twenty six (40.6%) patients reported symptomatic worsening during the lockdown period. Slowness in activities of daily living and walking worsened in 15 (57.7%) and 14 (53.8%) patients respectively while tremors increased in 12 (46.2%) patients. Mood and sleep disturbances were the most common non-motor symptoms to worsen. Increase in non-motor symptoms and the NMSS total score were independent predictors of PDQ-8 scores. Increase in non-motor symptoms during the lockdown was an independent predictor of the highest quartile of PDQ-8 SI scores.

Conclusions:: Conclusions-Motor and non-motor symptoms have worsened in PD patients during the lockdown. The increase in non-motor symptoms was independently associated with poorer quality of life among PD patients during the lockdown.
EMERGENCY DEPARTMENT ATTENDANCES FOR SEIZURES: THE SARS-COV-2 PANDEMIC IMPACT.

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Background and Aims:: The spreading of SARS-CoV-2 pandemic had an impact both on the healthcare organization and both on how people with COVID-unrelated acute and chronic conditions sought for medical assistance, in particular for condition requiring admission to Emergency Departments (EDs).

Methods:: We performed a retrospective study evaluating the frequency and features of ED attendances for seizures, in the University Hospital of Trieste, Italy, during the first lockdown period (March 10th-April 30th 2020). To define the possible pandemic impact, we compared the lockdown period to a matched period in 2019 and to a period of identical length preceding the lockdown (January 18th-March 9th 2020). Data were retrospectively collected: age, sex, triage code, admission by ambulance, required hospitalization, first seizure, seizure semiology and diagnostic tests performed (EEG or CT) of each patient.

Results::

![Graph showing ED admissions and associated data]

We found, during lockdown, a significant decrease in total ED attendances (4664) when compared to the matched control (10424) and to the pre-lockdown (9522) periods. Similarly, a reduction was detected for seizure attendances: 37 during lockdown and 63 and 44 respectively during the two other time periods. Interesting we found that more patients attended the ED with first seizures (p = 0.013), and a higher number of EEGs (p = 0.008) and CT brain scans (p = 0.018) were performed during lockdown; a trend favouring a more frequent transport to the ED by ambulance (p = 0.061) was also noted during lockdown period.

Conclusions:: The pandemic had a relevant impact on how patients with seizures accessed the ED.
THE PARADOXICAL IMPACT OF COVID-19 ON PEOPLE WITH POSTSTROKE APHASIA

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Background and Aims:: The coronavirus pandemic (COVID-19) is affecting people’s health with severe psychological consequences. One of the leading causes of long-term post-stroke disability worldwide is Aphasia. The language deficits of person with aphasia (PWA) cause a long-lasting negative impact on social communication and psychosocial wellbeing. The aim of the current study was to analyze the impact of the COVID-19 outbreak in PWA.

Methods:: 73 post-stroke PWA and 81 matched controls were enrolled in this study. All patients were in the chronic phase and they were already discharged from rehabilitation services before the COVID-19 emergency with different degrees of linguistic impairments. All participants were administered the Hospital Anxiety and Depression Scale (HADS). PWA also completed the Stroke and Aphasia Quality of Life Scale-39 (SAQOL-39).

Results:: In all participants, results showed a significant increase of depression and anxiety between pre and during COVID-19. Surprisingly, we found lower levels of depression and anxiety in PWA than in the healthy group. Moreover, a significant deterioration was also present in PWA in the communication and psychosocial scales of the SAQOL-39. Interestingly, these findings were independent of the degree of aphasia severity.

Conclusions:: This evidence masks a dramatic situation which affects post-stroke PWA. Given that language deficits severely impact on social communication and psychosocial wellbeing in this population, these conditions had paradoxically limited the effects of the coronavirus. Thus, our findings point to the urgency of implementing new tools, including telerehabilitation, which would allow PWA to practice their communication skills avoiding further deterioration.
UNRAVELING THE NEUROPSYCHOLOGICAL DISORDERS IN THE POST-COVID 19 SYNDROME: DYSEXECUTIVE SYNDROME AND SUBJECTIVE COGNITIVE COMPLAINT

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Background and Aims:: A considerable amount of recovered COVID-19 patients complain of long-term cognitive sequelae mainly in attention and memory. However, most of the few previous studies failed to clarify these cognitive syndromes, and their etiopathogenesis is much debated. The aim of this report is to contribute to the identification of the neuropsychological disorders in the post COVID-19 syndrome, and hypothesize a putative underlining etiopathological mechanism.

Methods:: Two male adult patients underwent standard and computerized neuropsychological assessment two months after recovery from COVID-19 interstitial pneumonia. Case 1 suffered a severe SARS, requiring CPAP and helmet NIV, and reported episodes of heart failures. Case 2 instead reported a mild SARS that was treated with oxygen therapy.

Results:: Both patients complained of mental fatigue, slowness, decreased concentration, and memory failures. Case 1 cognitive evaluation showed mild impairments in working memory, processing speed, short-term and episodic memory, while it was normal in Case 2. Both patients had mild mood abnormalities. No neuroimaging examinations were conducted yet at that time.

Conclusions:: The cognitive profiles of our patients were compatible with a mild dorsolateral dysexecutive syndrome in Case 1, and a subjective cognitive disorder in Case 2. The results suggest impairments of the dorsolateral prefrontal cortex and subcortical circuitry in both cases. The severity of the cognitive outcomes seems to be associated with the severity of SARS but not with mood disorders. We cautiously hypothesize that both patients might have suffered cognitive failure as a consequence of subclinical hypoxic insult to the brain.
DIFFERENTIAL DIAGNOSIS OF CACOSMIA AND DYSGEUSIA IN COVID-19 PANDEMIC. CLINICAL CASE REPORT.

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Emergency Institute, Neurology, Chisinau, Moldova

Background and Aims:: Olfactory and gustatory dysfunctions were presented in a high percentage of COVID-19 cases. Most of them are represented by quantitative disorders. Qualitative alterations were established in a small proportion. During the Covid-19 pandemic, there is a need to make a differential diagnosis (DD) of olfactory and gustatory disorders.

Methods:: Clinical case of a 64-year-old man presented with dairy food cacosmia and dysgeusia for the last two weeks, and night sweats. From medical history we found that our patient recovered from COVID-19 infection, one month ago.

Results:: Based on some studies, patients with COVID-19 infection, presented moderate to severe olfactory or gustatory dysfunctions for long-term, in convalescent period. It's important to make a DD of smell and taste impairments and choose the necessary treatment. Esophageal candidiasis was diagnosed in our patient. After 21 days of antifungal treatment cacosmia and dysgeusia disappeared. HIV test was negative. Some studies presented that COVID-19 infection is linked with a continuous reduction in lymphocytes along the disease. We hypothesized that immunodeficiency in COVID-19 infection and antibiotic therapy could be the trigger for esophageal candidiasis in our case.

Conclusions:: Our case report highlighted the importance of smell and taste disorders DD, in COVID-19 pandemic. Dairy food cacosmia and dysgeusia can be a sign of esophageal candidiasis. That's why, convalescent COVID-19 infection patients should be monitored for a long-term period.
COVID-19 RELATED ATAXIA AND MYOCLONUS: PARA- OR POST-INFECTIOUS DISORDER?

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¹Sant'Andrea Hospital, Department Of Neurology, La Spezia, Italy, ²Sant'Andrea Hospital, Department Of Neurology, La Spezia, Italy, ³IRCCS, Ospedale Policlinico San Martino, Department Of Neurology, Genova, Italy, ⁴IRCCS, Ospedale Policlinico San Martino, Department Of Anaesthesia And Intensive Care, Genova, Italy, ⁵IRCCS, Ospedale Policlinico San Martino, Nuclear Medicine Unit, Genova, Italy, ⁶IRCCS Ospedale Policlinico San Martino, Interventional Pulmonology Unit, Genoa, Italy, ⁷IRCCS Ospedale Policlinico San Martino, Autoimmunology Laboratory, Genova, Italy

Background and Aims:: Since the onset COVID-19 pandemic, several post-infectious neurological disorders have been reported, among which at least ten cases showed movement disorders consisting of tremor, myoclonus, ataxia. We report a case series of three patients who developed these symptoms after the SARS-CoV-2 infection.

Methods:: Patients' data were collected from medical records during COVID-19 pandemic. Diagnosis of COVID-19 was supported by RT-PCR on nasopharyngeal swab.

Results:: Three male patients (mean age 63 years) developed generalized myoclonus and ataxia. In two patients the disorder appeared 30 and 24 days after the onset of the SARS-CoV-2 infection, respectively, while in the other case the neurological symptoms began at the same time. The clinical pictures showed a rapidly worsening course. Brain MRI did not reveal abnormalities in any patients at the disease onset. On day 70 the imaging control showed mild cerebellar atrophy in one patient. A brain¹⁸F-FDG-PET scan disclosed a bilateral fronto-mesial hypometabolic pattern in one patient. RT-PCR for SARS-CoV-2 in CSF, tested in two cases, resulted negative. EEG and ENG did not reveal relevant abnormalities, as well as CSF analysis, including immunoblot. Two patients were treated with intravenous immunoglobulin infusion (IVig) and one patient with plasmapheresis (PEX). They subsequently improved during the course of few weeks.

Conclusions:: Myoclonus and ataxia possibly occur as COVID 19 postinfectious as well as parainfectious immune-mediated disorder. Indeed, IVIG or PEX were effective in all three patients. This kind of disorders have been described as postinfectious events, in contrast, we report, to our knowledge, the first parainfectious case.
A CASE OF LIMBIC ENCEPHALITIS WITH CSF DETECTION OF SARS-COV2 VIRUS: IMMUNE-MEDIATED MECHANISM OR DIRECT VIRAL DAMAGE?

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Background and Aims:: Pathogenesis of neurologic syndromes COVID 19-related could be categorized in four mechanisms: direct viral damage, para/post-infectious effect, complications of prolonged illness. We present a case of limbic encephalitis (LE) with concurrent detection of SARS-CoV2 virus in cerebrospinal fluid (CSF), which makes the individuation of a unique etiological mechanism insidious.

Methods:: A 70-year-old man was hospitalized with respiratory symptoms and confusional state. A chest CT-scan and nasopharyngeal swab demonstrated COVID-19 infection; non-contrast brain CT-scan was unremarkable. Neurological examination revealed right focal signs and vigilance fluctuations; EEG showed nonspecific mild background activity slowing, basic CSF investigations resulted negative and total-body CT-scan excluded tumours. Brain MRI showed T2-FLAIR hyperintensity in the mesial temporal lobes, strongly supporting the hypothesis of limbic encephalitis. So the patient underwent to a second lumbar puncture to test the autoimmune panel (negative).
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Results: Liquoral PCR for SARS-CoV2 RNA resulted positive. After treatment with 5 days- IV bolus dose of metiprednisolone and a cycle of IV immunoglobulin therapy, he had a slight improvement, especially concerning alertness and cognition. Two months follow-up brain MRI was superimposable to the precedent.
Conclusions: Majority of cases of LE with positive testing for specific antibodies are negative for RT-PCR for SARS-CoV2 tested on LCR(1). In this case, the presence of the virus in CSF supports a direct neural damage; conversely, the answer to immunomodulant treatment could suggest an immunological role; previous autopsy results of patients with SARS-CoV1(2) evidenced the presence of viral RNA in brain tissue, particularly accumulating in and around the hippocampus.

Background and Aims: In addition to the problems it causes in the acute phase, coronavirus infection is bothering physicians and scientists worldwide with its complex complications. Aim: To analyze the complications and clinical manifestations observed in the maxilla-facial area of patients who have undergone Covid-19.

Methods: Clinical analysis was carried out in 67 patients who visited to the multidisciplinary clinic of Tashkent Medical Academy for 6 months. The mean age of patients was 61±2.3 years, including 38 women (56.7%) and 29 men (43.3%). Patients were hospitalized 1-3 months after the onset of acute Covid-19 infection. The analysis was based on patients’ clinical status, medical history, complaints, and diagnosis.

Results: Mild complication observed in patients: acute aphthous stomatitis developed in 12 (17.9%) patients, in 29 (43.2%) patients inflammatory infectious complications (abscess, phlegmon) in the soft tissues developed independently. Inflammation of salivary glands was found in 7 (10.4%) patients, 36 patients (53.7%) had osteomyelitis of the maxilla (im.1), 37 patients (55%) were hospitalized with cavernous sinus thrombosis (im.2).

In addition to inflammation, patients had neurological symptoms including headache, dizziness, and so on. Facial nerve paresis in 14 (21%) patients, paresthesia of the trigeminus nerve in 28 (41.8%) patients (n. ophthalmicus - 38 (57%), n. maxillaris - 40 (60%), n. mandibularis - 2 (3%)), paresthesias of the 1st and
2nd horn together in 41 (61%) patients.

Conclusions:: Considering that Covid-19 disease leads to severe and long-term complications in the late stages, it is needed to develop measures to prevent complications in patients with predisposition to complications (elderly and chronic comorbidities)
SPONTANEOUS INTRACEREBRAL HEMORRHAGE AFTER ANTICOAGULATION THERAPY IN A 57-YEAR-OLD MAN WITH SARS-COV-2 INFECTION: A CASE REPORT

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\textbf{Background and Aims::} Anticoagulation regimens are now being considered for COVID-19. Anticoagulation is known to increase the risk for adverse bleeding events, of which intracerebral hemorrhage (ICH).

\textbf{Methods::} Case Report

\textbf{Results::} We report a 57-year-old man was admitted to hospital due decreased oxygen saturation, increased blood glucose levels and RT-PCR of oropharyngeal swab confirmed COVID-19. The patient had a previous history of type 2 DM and ischemic stroke. The first 5 days, the patient was receiving a prophylactic dose of low molecular weight heparin, enoxaparin, then continued with unfractionated heparin. The patient also received antiplatelet clopidogrel and convalescent plasma. The laboratory results are leucocyte 18.9 K/\mu\text{L}, ureum 79 mg/dL, creatinine 2.0 mg/dL, D-Dimer 0.22 \mu\text{g/mL}, INR 1.03, NLR 15.82, ALC 547, HbA1C 9.2, blood glucose level 336 mg/dL, CRP 41.2 mg/dL. On day ten of hospitalization, the patient had sudden right-sided hemiplegia and Broca's aphasia. A CT head demonstrated an ICH in the left basal ganglia with a volume approximately 77cc. Three days later the patient's condition had decreased consciousness and a craniotomy was performed. After being intubated for 4 days post craniotomy, because his condition improved, he was extubated. On day nine after surgery, the patient's condition decreased to coma, a repeat chest X-ray showed a worsening of the bilateral infiltrates and pleural effusion. His oxygen requirement was progressively increasing, so he was shifted to mechanical ventilation again.

\textbf{Conclusions::} The risk of intracerebral hemorrhage in patients with COVID-19 is of paramount importance to inform the risk-benefit assessment of the use of anticoagulation in this patient.
CLINICAL ANALYSIS OF COMPLICATIONS OF CAVERNOUS SINUS THROMBOSIS IN COVID-19 PATIENTS

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Background and Aims:: Serious complications such as cavernous sinus thrombosis have been reported in patients with coronavirus disease. Objective: to study and analyze the clinical course of cavernous sinus thrombosis in patients who underwent Covid-19

Methods:: Clinical analysis performed in 52 patients who applied to the multidisciplinary clinic of Tashkent Medical Academy over a period of 10 months. The mean age of patients was 60 ± 3.5 years, of them 28 women (53.8%) and 24 men (46.2%). The patients were hospitalized 1-2 month after infection, all tested positive for coronavirus (PCR, IFA). Clinical and laboratory examination of the patients, MRI-angiographic studies, medical history, complaints, and diagnosis were performed.

Results:: According to analysis, septic cavernous sinus thrombosis was 75-80% and aseptic cavernous sinus thrombosis was 20-55%. Notably, the predominance of neurological symptoms in patients was unilateral in the head and face, unilateral chronic hemorrhagic sinusitis, and unilateral eye socket syndrome, loss of eyesight. In patients, despite complex treatment, the inflammatory process was chronic. In the process of inflammation we noted 38% of cases of soft tissue phlegmon, 70% of cases of transient necrosis with aseptic inflammation of the upper jaw, 55% of cases of orbital phlegmon (pictures). Patients complained of headache (85%) and general weakness (77%), discomfort (72%), loss of sensitivity in face - 70%, mouth cramps (100%), facial nerve palsy
Conclusions: in complication in patients with Covid-19 cavernous sinus thrombosis the process is characterized by progressive development on one side of the head and face. Complex treatment of patients requires multidisciplinary rehabilitation measures
BEHAVIOR AND AWARENESS OF MULTIPLE SCLEROSIS PATIENTS DURING COVID-19 PANDEMIC IN A TERTIARY CENTER IN EGYPT

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¹Cairo University, Neurology, Cairo, Egypt, ²Cairo University, Neurology, Cairo, Egypt

Background and Aims:: Knowing that assessing patient awareness and knowledge about the coronavirus is important in recognizing gaps and offering better efforts especially in patients with chronic illness like MS patients, this study aims to investigate the knowledge, attitudes and practices of MS patients during COVID-19 pandemic.

Methods:: A telephone-based survey which recruited patients from Kasralainy Multiple Sclerosis Unit database, Cairo University hospitals from March 2020 till July 2020. It included 127 patients and an Arabic questionnaire was conducted which consisted of 14 questions including: Demographic data; MS related data, Data related to COVID-19 and attitude and awareness related to COVID-19

Results:: Near quarter of the patients were still working in their current jobs, only 12.8% on current leave due to Covid-19 while the majority were non-employed (66.4%). The majority of patients (64%) were compliant to their medications. Treating physician advised to stop DMT in 20.4% while 10.2% of patients stopped due to fear of side effects. Only 16.54% of the patients developed COVID-19 symptoms. The majority (89.2%) avoided visiting any medical institution. Different ways of communication were used by patient when any medical advice was needed. Facebook and WhatsApp applications represented almost half of the tools used to communicate.

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Conclusions:: Patients with MS report increased awareness of COVID-19 precautions with high rate of DMT compliance.
Background and Aims:: The ongoing coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus (SARS-CoV)-2 is having unprecedented effects in healthcare systems, economies and society. Although the respiratory tract is the primary target of SARS-CoV-2, emerging evidence suggests that the virus may also invade the central nervous system (CNS), leading to numerous neurological issues. In particular, people with Alzheimer’s disease (AD) are vulnerable group at risk of contracting COVID-19 and present more severe forms and worse outcomes. Given the high prevalence of AD individuals affected by COVID-19, the aim of was to review common underlying etiological factors that may contribute to the acceleration of neurodegenerative processes in SARS-CoV-2-infected patients.

Methods:: PubMed database was searched for publications before 1st April 2021 using the keywords: “Alzheimer’s disease” AND “COVID-19” AND “SARS-CoV-2”.

Results:: Inflammatory biomarkers, including IL-1, IL-6 and galectin-3 (Gal-3) are associated with high risk for developing COVID-19 and with the progression of AD. Moreover, SARS-CoV-2 infection exhibit high plasma levels of neurofilament light chain protein (NfL) and glial fibrillary acidic protein (GFAP), known as biochemical indicators of neuronal injury and glial activation in AD. Interestingly, the presence of the Apolipoprotein E (APOE) ε4 allele represents a risk factor for both diseases.

Conclusions:: Current literature suggests the existence of a synergistic relationship between COVID-19 and AD. The identification of potential biomarkers for the early identification of COVID-19 in patients with high risk of developing AD as well as the management and development of novel therapeutic strategies against both diseases.
RISK FACTORS FOR COVID-19 VACCINE HESITANCY AT A NEUROSCIENCE CENTER: QUALITY IMPROVEMENT SURVEY

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¹University of Hawai‘i at Mānoa, John A. Burns School Of Medicine, Honolulu, United States of America, ²Hawaii Pacific Neuroscience, Clinical Research Center, Honolulu, United States of America

Background and Aims:: This quality improvement (QI) survey aimed to identify risk factors for COVID-19 vaccine hesitancy among patients with a neurological disorder.

Methods:: A telephone QI survey was conducted of randomly selected adult Hawaii Pacific Neuroscience patients between January 22 and February 13, 2021. The survey assessed vaccine perception in relation to over 30 sociodemographic variables and medical comorbidities. Nonparametric univariate and multivariable logistic regression models with alpha < 0.05 were utilized.

Results:: From the 1494 patients contacted, 363 were respondents, with 81.34% planning to vaccinate. Odds of COVID-19 vaccination acceptance were significantly lower for patients on Medicaid (0.42, IQR: 0.22, 0.82; $X^2 = 7.18, p = 0.0074$), with drug use (0.32; IQR: 0.11, 0.96; $X^2 = 4.73, p = 0.030$), whose primary source of COVID-19 information was social media (0.26, IQR: 0.11, 0.63; $X^2 = 10.71, p = 0.001$), and who did not receive the most recent influenza vaccine (0.20, IQR: 0.11, 0.36; $X^2 = 33.38, p = 7.57 \times 10^{-9}$). After multivariable logistic modeling, the best predictors of declination were use of social media as a primary source of COVID-19 information, concerns of vaccine safety, self-perception of a preexisting condition compromising vaccination safety, not receiving the influenza vaccine within the past year, having completed some high school education, being a current smoker, and having no history of cerebrovascular accident.

Conclusions:: Patients with neurologic disorders present with unique risk factors for vaccine hesitancy, which may require special attention and vaccine counseling.
COGNITIVE IMPAIRMENT IN PREVIOUSLY INDEPENDENT COVID-19 PATIENTS: THE TIP OF THE ICEBERG?

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Mons. Luigi Novarese Hospital, Dept. Of Rehabilitation, Moncrivello (VC), Italy

Background and Aims:: Several pathologies other than pulmonary disease have been attributed to COVID-19. No data are available on the cognitive status of postCOVID-19 subjects without a history of cognitive impairment.

Methods:: Out of 285 subjects admitted to the Internal Medicine COVID Unit from November 2020 to January 2021, 48 patients [median age=73.5(23.25); 24M/24F] were recruited and evaluated with MoCA Test HAM-D, HAM-A; an evaluation of blood oxygen saturation and heart rate was performed before and after the assessment. Inclusion criteria were: radiologically confirmed symptomatic COVID-19 pneumonia, positive reverse transcription-polymerase chain reaction nasopharyngeal swab, being independent at home before the infection (Barthel Index=100), not being previously diagnosed with cognitive impairment/neurological diseases, no delirium episodes during COVID-19 acute phase, no mechanical ventilation need and no oxygen supplementation at the time of evaluation.

Results:: The median score of MoCA test was 20.5(8) and no subjects showed relevant anxiety [median HAM-A score=5.5(9)] and/or depressive symptoms [median HAM-D score=5(7.5)]. According to MoCA score, the sample was divided into two groups: 34 subjects with MoCA<23 (Impaired Group) and 14 subjects with MoCA≥23 (Normal Group). MoCA was correlated to age (p=0.0002; b=-0.571).

Conclusions:: The MoCA reveal that cognitive impairment is present in previously independent subjects and it is more detectable in subjects older than 65 years compared to younger. No data are available to determine whether COVID-19 will lead to cognitive dysfunction related to the sub-acute phase of the infection or to an increase of long-term cognitive impairment, therefore a follow-up will be crucial.
COGNITIVE AND NEUROPSYCHIATRIC FEATURES OF COVID-19 PATIENTS AFTER HOSPITAL DISMISSION: AN ITALIAN PILOT STUDY

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Moriggia Pelascini Hospital, Department Of Parkinson’s Disease, Movement Disorders And Brain Injury Rehabilitation, Gravedona ed Uniti, Italy

Background and Aims: Recent studies suggest cognitive, emotional, and behavioral impairments occur in patients after SARS-CoV-2 infection. However, studies are still few and to our knowledge, without a control group. This study aims to assess the prevalence of neuropsychological and neuropsychiatric impairment in patients after hospitalization.

Methods: We enrolled 17 Covid+ patients (M/F:12/5; age: 53,59±12,32yrs; education 11,88±3,6yrs) who needed hospitalization but no IC, about 18 days post dismission, and 17 Covid- matched controls (M/F:11/6; age: 53,82±12,34yrs; education: 12,59±3,77yrs). Neuropsychological and neuropsychiatric assessments were conducted via teleneuropsychology with the following tests: MMSE, CPM47, RAVLT, CDT, Digit-Span Forward/Backward, Verbal fluencies; BDI-II, STAI, AES. People with previous cognitive impairment, neurological or psychiatric conditions were excluded. Clinical and demographics were collected. Comparison between groups was conducted using parametric or non-parametric tests according to data distribution (T-test, Mann Withney-U test; Chisquare).

Results: Among Covid+, 82% had at least one pathological test (vs 30% in Covid-: p=0,001) and significantly worst performances than Covid- in Digit Backward (4,05±1,2 vs 4,8±1 p=0,046), RAVLT Learning (42±9,4 vs 49,4±7,9 p=0,018), RAVLT Recall (8,1±2,9 vs 10,6±2,5 p=0,013), Semantic Fluencies (43,7±7,3 vs 50,6±6,8 p=0,008). STAI-Y2 was higher in Covid- (32,6±7,4 vs 40,5±7,9 p=0,005).

Conclusions: Patients Covid+ assessed by teleneuropsychology showed a vulnerability in some memory and executive functions (working memory, learning and recall, semantic memory). Intriguingly, anxiety was higher in the control group. Our findings, therefore, confirm an impact of Covid-19 on cognition even in patients who did not need IC. Follow-up is needed to evaluate if these difficulties can recover with time.
COGNITIVE AND AFFECTIVE DISORDERS IN CRITICAL SARS-COV-2 PATIENTS AND CAREGIVERS

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Background and Aims:: We investigated cognitive and affective disorders in patients with SARS-CoV-2 hospitalized in Intensive Care Unit (ICU). Caregivers quality of life, psychological distress and satisfaction with the information received by health-care professionals were assessed.

Methods:: From March 1 to April 30, 2020, 22 consecutive patients with SARS-CoV-2 infection, confirmed by PCR on oronasopharyngeal swab, requiring ICU admission were recruited together with a caregiver. Patients with previous cognitive disorders were excluded. Three months after ICU discharge, patients underwent a comprehensive neuropsychological evaluation and filled out validated questionnaires.

Results:: Seven of 22 resulted mildly cognitively impaired. Memory was the most impaired domain, followed by attention and verbal fluency. Three out of 22 patients reported an average high level of anxiety but no depression. Quality of life was mild impaired for 19 patients. Lower performances at MoCA were related to higher APACHE score at T0 (r = -0.44; p < .04). Lower performances in working memory, short- and long-term memory and verbal fluency were correlated to longer ICU stay, duration of mechanical ventilation and longer treatment with opioid and antipsychotics drugs (r > -0.48; p < .04). Long term memory performances were related to higher Sequential Organ Failure assessment (SOFA) score and longer treatment with propofol and benzodiazepines (r > -0.53; p < .02). Higher patient’s anxiety was correlated to higher psychological distress of the caregiver (r = -0.64; p < .001). Higher SOFA score is related to lower caregiver quality of life and lower satisfaction with information received (r > -0.53; p < .02).

Conclusions:: At 3 months from ICU admission, cognitive and psychological distress sequelae can be observed in SARS-CoV2 ICU patients.
ITALIAN BOTULINUM TOXIN NETWORK RECOMMENDATIONS FOR SAFE TREATMENT OF BOTULINUM TOXIN INFILTRATION DURING THE COVID-19 PANDEMIC: A VIDEO PRESENTATION

Francesco Bono¹, Maria Concetta Altavista², Roberto Eleopra³, Appendix. On Behalf Of The Italian Botulinum Toxin Network safe Infiltration Project Participants: Albanese M.; Albani G.; Assetta M.; Autunno M.; Babbini M.T.; Balestrieri F.; Barbero P.; Barbieri S.; Bargellesi S.; Bentivoglio A.; Bertolasi L.; Bizza M.; Capone L.¹, Castagna Castagna A.; Castronovo G.; Cerchi A.; Cesaretti C.; Cevoli S.; Coletti Moja M.; Corradini C.; Crapanzano F.; Danni M.C.; De Bartolo M.; De Fazio G.; Del Colle R.; Doretti A.;¹, Fazio Fazio N.; Flamma G.; Frasson E.; Frontoni M.; Giorgianni R.; Girlanda P.; Grazzi L.; Inglese C.; Leggio U.; Lettieri C.; Liberi P.; Liotti V.; Lo Fermo S.; Lori S.; Lozza A.; Maggi L.; Maggioni G.;¹, Manpreso Mampreso E.; Manzo L.; Marchese R.; Marinelli L.; Masi G.; Milano E.; Misceo S.; Moccia M.; Osio M.; Petracca M.; Pascarella A.; Polidori L.; Pozzolante R.; Prudenzano M.P.; Romano M.C.;¹, Rossi Rossi V.; Sacco S.; Sances G.; Santoro A.; Scaglione Cesa L.; Sidoti V.; Soliveri P.; Squintani G.M.; Tambasco N.; Terranova C.; Torelli P.; Truscello C.; Valzania F.¹

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Background and Aims: Overview The physician and the patient come into close contact during treatments with botulinum toxin, increasing the chances of infection with the SARS-CoV-2 virus. What do we need to do to make the treatment safe and reduce the risk of contagion?

Methods: Botulinum toxin infiltration procedure Instructions for the Patient Wear non-sterile gloves and a surgical mask, and do not touch handles, surfaces or other objects. Dress and undress in the appointed place Instructions for the physician/paramedical staff Remove all jewelry and personal items, Wash hands for 20'', Put on PPE Physicians and nurses must put on a first pair of gloves, shoe covers, a cap, a disposable gown, an FFP2 mask, and protective glasses or a face mask and, lastly, a second pair of gloves.

Results: After treating each Patient the physician must remove the second pair of gloves, the disposable gown, and the protective glasses or face mask and sanitize them all. Lastly, he or she may remove the first pair of gloves. If the treatment takes place in the vicinity of the oral cavity, head or neck, the FFP2 mask must also be replaced. Medical Workers must clean all surfaces with which the Patient has been in contact at the end of each treatment session and, cover the most exposed surfaces with disposable barriers. As a final recommendation, the premises should be ventilated frequently.

Conclusions: Summary When these instructions are properly followed, they make the botulinum toxin infiltration procedure safe for the patient and the medical staff
BIOCHEMICAL BLOOD ANALYSIS OF PATIENTS WITH COVID-19 COMPLICATED BY Cavernous Sinus Thrombosis.

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Background and Aims:: Serious complications such as cavernous sinus thrombosis and osteonecrosis of the jaw have been reported in elderly and diabetic patients with covid-19. Dysmetabolism is a risk of developing such complications, severity of pathology and long-term treatment. Our aim was to study metabolic changes in the blood in diabetic patients suffered covid-19 complicated by cavernous sinus thrombosis.

Methods:: Clinical analysis was carried out in 52 patients who applied to the multidisciplinary clinic of Tashkent Medical Academy for 4 months. The mean age of patients was 60 ± 3.5 years, of them 28 women (53.8%) and 24 men (46.2%) with complications trombosis of cavernosis sinuses. Patients were hospitalized an average of 1 month after the onset of acute Covid-19 infection.

Results:: According to the analysis septic cavernous sinus thrombosis was 73.2%, aseptic cavernous sinus thrombosis - 26.8%. Biochemical analysis of the serum content of total protein and albumin was carried out, which caused the decrease of indicators to the lower limits of the norm in the blood. The mean increase in glucose was 13.7 ± 0.44 (r < 0.001), ALT (32 ± 0.24 U/L); AST (24 ± 0.44 U/L). creatinine was found the upper limit of norm. High-density lipoproteins (1.09 ± 0.16) decreased, and low- and very-low-density lipoproteins (4.78 ± 0.59) and atherogenicity indices were increased.

Conclusions:: Change in a number of biochemical parameters (hypoproteinemia, dyslipidemia) and other metabolic disorders can aggravate the severe course of the underlying disease. Metabolic disorders (dyslipidemia) leads to vascular occlusion, increases microcirculatory disorders, negatively affect the outcome of treatment.
THE BENEFIT OF A SHORT-STAY NEUROLOGICAL OBSERVATION UNIT IN THE COVID-19 ERA.

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Background and Aims:: Acute neurological symptoms are responsible for 5-15% of referral to the Emergency Department (ED). Since the COVID-19 outbreak, our stroke network shifted toward a mothership model with direct transport of stroke patients to the Comprehensive Stroke Center ("M. Bufalini" hospital, Cesena, Italy). To handle the increase in referrals due to mothership and guarantee a neurological fast-track in the ED, the Neurology service opened a four-bed Short-Stay Neurological Observation Unit (SSNO or “OBI Neuro”). We retrospectively analyzed the performances of SSNO after one year of activity.

Methods:: We evaluated one-year (1st April 2020 - 31st March 2021) SSNO patients’ admissions, discharge destinations, diagnosis and mean length of stay.

Results:: We managed 556 patients in the SSNO. Of these, 280 (50.4%) were discharged at home, 248 (44.6%) were admitted as in-patients, 20 (3.6%) were transferred to other hospitals, 8 (1.4%) self-discharged. Among patients admitted as in-patients, 91 (36.7%) were admitted in the Neurology ward, 135 (54.4%) were admitted in the Stroke Unit, the remaining (8.9%) in other wards of the hospital. The most common diagnoses were stroke (32.3%), seizure (20.4%), TIA (13%) and headache (7.4%); all other diagnoses individually represented less than 5% of the total. The mean stay of length was 11.5 h (14.4 h for discharged patients and 7.3 h for admitted as in-patients).

Conclusions:: The SSNO was feasible and strategic in managing stroke referrals in a mothership model and lifting the burden of neurological patients from the ED during the COVID-19 pandemic.
Background and Aims:: Acute Disseminated Encephalomyelitis (ADEM) is an immune-mediated demyelinating disease of the Central Nervous System clinically defined by acute polyfocal neurological syndrome usually following a monophasic course. ADEM often occurs after infections, but 5-10% of cases are preceded by vaccinations. Several cases of ADEM after SARS-CoV-2 infection have been described, whereas no cases have been reported after administration of mRNA/adenovirus COVID-19 vaccines. Here, we describe a suspected case of ADEM presenting two weeks after receiving the first dose of ChAdOx1 nCoV-19 vaccine.

Methods:: Case report

Results:: A 45-year-old man developed numbness in his hands two weeks after receiving the first dose of ChAdOx1 nCoV-19. His condition worsened in a few days: numbness extended to the upper limbs, trunk and legs and he progressively experienced visual acuity deficits, dysarthria, dysphagia, clumsy right hand movements and urge incontinence. Symptoms persisted for one week but then spontaneously improved. At admission to our unit, MRI showed large T2-weighted hyperintensities in the pons (which appeared swollen), right thalamus and multiple spinal cord segments. All lesions, except the thalamic and a single spinal area, were contrast-enhancing. Cerebrospinal fluid revealed mild lymphocytosis with no tumor cells or infectious agent detected at PCR. Serology for infectious/autoimmune diseases and total-body CT resulted negative. Clinical and neuroradiological improvement ensued right after a 5-day course of high-dose IV methylprednisolone.

Conclusions:: The diagnostic work-up suggests a diagnosis of ADEM, a disease whose association with vaccines is well-known. This is the first description of a possible association with an adenovirus COVID-19 vaccine.
CHARACTERISTICS AND OUTCOMES OF COVID-19-RELATED STROKES: A RETROSPECTIVE STUDY IN A TERTIARY HOSPITAL

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Background and Aims:: The hypercoagulable state that the COVID-19 elicits can lead to acute thrombotic complications including ischemic stroke. Here we describe the clinical profile, neuroimaging findings, interventions, and outcomes of COVID-19-related stroke patients in a tertiary hospital.

Methods:: This is a retrospective study of all COVID-19-related stroke patients who were hospitalized between November 2020 and March 2021 at King Abdullah University Hospital (KAUH) during the peak period in Jordan. Clinical characteristics, laboratory and neuroimaging data, interventions, and outcomes were collected. SARS-CoV-2 infection was confirmed in all patients by RT-PCR testing.

Results::

\[
N = 17
\]

- Minor (0-4): 5
- Moderate (5-15): 9
- Severe (21-42): 3
A total of 17 COVID-19-related stroke patients were identified, with a mean age of 70.8 ± 9.4 years and a male percentage of 47.1% (8/17). All of them were ischemic strokes. COVID-19-related stroke patients had high peak D-dimer and troponin levels with a median of 4.13 (IQR: 11.81), and 0.041 (IQR: 0.105), respectively. The mean duration of hospital stay was 11.9 ± 9.2 days. Seven patients died in the hospital (41.2%), while 10 patients had a modified Rankin score of ≤ 4 at discharge. 

**Conclusions:** Cryptogenic and cardioembolic stroke patients were more severe with higher mortality and morbidity rates in comparison with other COVID-19-related strokes. Further studies are needed to determine the safety and efficacy of therapeutic and prophylactic anticoagulants in stroke patients with COVID-19 infection.
PATIENT SATISFACTION WITH TELEVISIT IN CHRONIC NEUROLOGIC DISORDERS DURING COVID-19 PANDEMIC

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Background and Aims:: Covid-19 pandemic has boosted telemedicine in medical clinical practice. Experiences in the management of chronic neurological disorders are limited as well as patient opinion. During Covid-19 pandemic we evaluated patients' satisfaction and opinion about televisits in a large group of patients with chronic neurological disorders.

Methods:: All patients with chronic neurological disorders who had a virtual visit during the first phase of pandemic were invited to fill an online anonymous questionnaire about their global satisfaction and regarding the following issues: continuity of care, possibility to stay at home, doctor-patient relationship, the future of teleconsultation after pandemic and understanding of medical informations.

Results:: We received 123 questionnaires among 232 e-mail (response rate 53%). Almost all (120 out of 121 patients, 99%) were satisfied with the overall experience with video-consultation. Comprehension of medical information was the same for 113 out of 122 patients (93%) and also the doctor-patient relationship was the same for 107 out of 122 respondents (88%) or better for 10 (8%). Ninety-three percent of patients (112 out of 120) were keen to integrate televisits with the traditional modality and only 11 out of 121 patients (9%) judged televisits as an option to discard. As a whole 114 out of 122 respondents (93%) would suggest this modality to other patients.

Conclusions:: Our large cohort of patients with chronic neurologic disorders rated experience with televisits satisfactory. Comprehension of medical information and doctor-patient interaction was considered good. Eventually patients are keen to integrate this modality with traditional follow-up visits.
NO IMPACT OF COVID-19 LOCKDOWN ON CLINICAL STATUS OF ELDERLY WITH COGNITIVE IMPAIRMENT OR DEMENTIA USING A STRUCTURED PHONE-BASED ASSESSMENT

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Background and Aims:: Aim of the study was to investigate by a standardized telemedicine protocol the impact of prolonged lockdown on cognitive and behavioral symptoms of dementia (BPSD) in a consecutive series of patients with cognitive decline.

Methods:: The study was carried out in patients with dementia who were periodically visited at the CDCD of ASST Spedali Civili. This study took place from April 01 to May 31 2020.Among the information collected: Clinical Dementia Rating Scale, a telephone version of Mini Mental State Examination (Itel-MMSE), the NPI-Q. The Perception of quality of life was investigated by both the caregiver and the patient (EQ5D) and by the Zarit Burden Inventory.

Results:: Overall, 90/108 completed the evaluation and the final sample included 52/90 females, with mean age 78.9 (SD 7.3), mean education 7.8 (SD 3.8) and mean duration of disease of 3.5 (SD 1.9) years. A significant aggravation since last in presence visits was found in 34/90 patients (37.1%), largely coincident with caregivers reporting (27/34, 79,%). A significant difference between the two groups was observed on NPI-Q stress scale (p<.0001) and on Zarit Burden Inventory (p<.0001). By logistic analysis, caregivers’ stress was significantly associated with patient CIRS score, duration of illness and NPI-Q total score at baseline

Conclusions:: This is one of the few studies to investigate the impact of SARS-CoV-2 related lockdown by comparing cognitive, functional and behavioral data collected by telemedicine. According to this study, patients did not suffer a significant clinical impact but multimorbidity, duration of illness and severity BPSD at baseline predicted caregivers distress.
THE EFFECTS OF THE COVID-19 PANDEMIC AND QUARANTINE MEASURES ON THE LIFESTYLES AND MENTAL HEALTH OF OLDER ADULTS AT INCREASED RISK OF DEMENTIA.

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Background and Aims:: A complete lockdown was adopted in Italy in Spring 2020 to limit the spread of the COVID-19 pandemic. Older adults, especially those with mild cognitive impairment (MCI), may be particularly prone to adopt unhealthy lifestyles and suffer mental health consequences from quarantine. This study aimed to explore the impact of COVID-19 and quarantine on lifestyles and mental health of seniors at increased risk of dementia.

Methods:: 126 Community-dwelling seniors with subjective cognitive decline or MCI (56%) were twice phone-interviewed 6-8 weeks after the lockdown beginning and 6-months later, after the easing of quarantine measures and school reopening. Data regarding health and COVID-19-related variables, cognition, depression, anxiety, apathy, physical activity (PA), mediterranean diet (MD), and leisure activities (LAs) was collected.

Results:: During lockdown, over 1/3 of participants reduced PA and MD adherence; 1/6 decreased mental-stimulating LAs; 1/5 were depressed, 1/10 anxious and 1/10 apathetic. Around 60% of them completed the second interview: almost 9/10 reported having not returned to pre-pandemic daily habits, 45% took less care of their health than before COVID-19. Compared to quarantine, only 16% increased PA and 21% increased adherence to MD, 81% resumed social LAs, but 45% decreased mental-stimulating LAs. Prevalence of depression and anxiety did not change significantly, while apathetic individuals nearly tripled and 72% of respondents achieved higher apathy scores compared to their first interview.

Conclusions:: The quarantine and protracted COVID-19 emergency led seniors to unhealthy lifestyles - which were mostly maintained even after reopening - and increased apathy, which may impact on their future risk of dementia.
FACEMASK HEADACHE: A NEW NOSOGRAPHIC ENTITY AMONG HEALTHCARE PROVIDERS IN COVID-19 ERA

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Background and Aims:: SARS-CoV-2 is a novel infectious agent causing Coronavirus disease 2019, which has been declared as pandemic in March 2020. Personal protective equipment has been mandatory for healthcare workers in order to contain the outbreak of pandemic disease. Mild neurological disturbances such as headache have been related to the extensive utilization of facemask. This study aims to examine headache variations related to the intensive utilization of facemask among a cohort of healthcare professionals in a setting of low-medium risk of exposure to SARS-CoV-2.

Methods:: This is a cross-sectional study amongst healthcare providers from different hospital and clinics in Italy. Each participant completed a specifically-designed self-administered questionnaire. Headache features and outcome measures' change from baseline were evaluated over a four-months period, in which wearing facemask has become mandatory for Italian healthcare workers.

Results:: A total of 400 healthcare providers completed the questionnaire, 383 of them met the inclusion criteria. The majority were doctors, with a mean age of 33.4±9.2 years old. Amongst 166/383 subjects, who were headache free at baseline, 44 (26.5%) developed de novo headache. Furthermore, 217/383 reported a previous diagnosis of primary headache disorder: 137 were affected by migraine and 80 had tension-type headache. A proportion (31.3%) of these primary headache sufferers experienced worsening of their pre-existing headache disorder, mainly for migraine frequency and attack mean duration.

Conclusions:: Our data showed the appearance of de novo associated facemask headache in previous headache-free subjects and an exacerbation of pre-existing primary headache disorders, mostly experienced by people with migraine disease.
COVID-19 INFECTION, DEPRESSION, AND ISCHEMIC STROKE

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Background and Aims:: Many recent studies have shown increasing evidence connecting COVID-19 infection with acute thrombotic events, and in particular with ischemic strokes. There are several theories regarding this association, such as alterations in lipid metabolism or platelet aggregation, injury of the endothelial cells, or massive cytokine release, leading to cytokine storm and hypercoagulation. The biological and social consequences of this infection can also lead to psychiatric afflictions, most frequently anxiety and depression being described. This study aims to highlight the possible connections between COVID-19 infection, depression, and ischemic stroke.

Methods:: We observed the case of a 48-year-old patient who presented with left hemibody paresthesia and motor deficit on the left side of the body. Two months prior, he presented a COVID-19 infection, followed by a major depressive episode. Clinical, neurological, and neuroimaging examinations were performed to establish the diagnostic. We also analyzed the existing risk factors and possible etiologies. The patient had a history of hypertension, hypercholesterolemia, obesity, and smoking.

Results:: Following investigations, the diagnosis of acute ischemic thalamic stroke was established. Although there have been more risk factors identified, a causative event that led to the decompensation of these conditions was searched. The post-COVID-19 infection status and recent depression episode represent reasonable presumptive causal factors.

Conclusions:: The relation between the acute ischemic thalamic stroke, previous COVID-19 infection, and subsequent depressive episode was considered to be plausible.
ROLE OF AN INTENSIVE INPATIENT REHABILITATION PROGRAM IN FUNCTIONAL RECOVERY AFTER GUILLAIN-BARRE’ SYNDROME RELATED OR NOT TO COVID-19

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Background and Aims:: Several cases of Guillain-Barre Syndrome (GBS) have been related to COVID-19, without data on the functional outcome after intensive rehabilitation. We aimed at presenting the results of rehabilitation in patients with COVID-19-related or not GBS.

Methods:: All the patients admitted in 2020 for GBS in a rehabilitation facility have been evaluated with Barthel index (BI), GBS-Disability Scale (GBS-DS) and Medical Research Scale-Sum Score (MRC-ss) at admission and at discharge, after an intensive rehabilitation program.

Results:: In 2020, three COVID-19-related (3F; mean age 72.33 years) and five non-COVID-19-GBS (2M/3F; mean age 73.2 years) were admitted. In non-COVID-19-GBS a high Acute Motor Axonal Neuropathy (AMAN) prevalence was detected [4 AMAN, 1 AMAN/Acute Inflammatory Demyelinating Polyradiculopathy (AIDP) mixed form]. Non-COVID-19-GBS experienced a high complications rate, with two deaths due to sepsis. At discharge, BI ameliorated in the three survivors (0-65, 35-70; 5-20) as MRC-ss (15-38; 43-52; 33-48). GBS-DS decreased in only two cases (4-2; 4-2; 4-4), with one patient regaining independent walking. COVID-19-GBS (2 AIDP, 1 AMAN) did not experience complications. Two AIDP patients recovered autonomous walking at discharge, with BI (25-95; 35-85) and MRC-ss (48-60; 36-59) rising, and GBS-DS decreasing (3-2; 3-2). In the only AMAN form, a light augment in BI (5-15) and MRC-ss (36-40) was noticeable, without GBS-DS reduction GBS-DS (4-4).

Conclusions:: COVID-19-related GBS had a better clinical outcome than non-COVID-19-GBS. However, epidemiological considerations cannot be deemed due to the small sample. More follow-up studies are warranted for the functional recovery evaluation of these patients.
PROLONGED COGNITIVE DEFICITS AFTER COVID-19

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Background and Aims:: Cognitive deficits are a common complication of COVID-19. Multiple factors associated with the illness and its treatment may contribute to cognitive deficits. In this study, we analysed neuropsychological data from a cohort of patients recovering from COVID-19 hospitalization who required different types of oxygen/ventilation therapy.

Methods:: We recruited 77 (aged 22–77 years; 57 males) patients hospitalized for complications of SARS-CoV-2 infection in different COVID units, which had required different oxygen (O₂) therapy (no-O₂ = 9, low-flow O₂=35, CPAP=26, intubation=7). Participants underwent neuropsychological testing with the Brief Repeatable Battery of Neuropsychological Tests (BRB-NT) about 5 months after hospital discharge.

Results:: Of all participants, 64% showed deficits in at least one test of the BRB-NT; the most affected functions were processing speed (41.6% of participants) and delayed verbal recall (27.3%). O₂ therapy with CPAP was associated with worse verbal memory performance (p=0.033), compared to no-O₂ therapy. Attention and processing speed deficits were not associated with type of O₂ therapy (p=0.889), but correlated with thromboplastin (aPTT) ratio (r=0.298, p=0.019). Worse delayed visuospatial recall was associated with hyposmia (p=0.011) and dysgeusia (p=0.035).

Conclusions:: Cognitive deficits are frequent, persistent, and disabling even for five months following hospitalization for COVID-19. Therefore, neurological and neuropsychological monitoring should be put in place after discharge to help mitigate the effects of these symptoms, improving the quality of life of COVID-19 survivors.
THE NEUROLOGICAL MANIFESTATIONS OF COVID19, THE MOST EXTENSIVE REVIEW OF PUBLISHED CASE REPORTS

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Background and Aims:: The spectrum of neurological involvement in COVID-19 has been rapidly reported during this pandemic in order to support fellow colleagues in prompt identification and management. This is the most extensive review of published case reports of neurological manifestations of COVID19. The aim of this study is to assess the frequency of neurological manifestations and complications, identify the neurodiagnostic findings, and compare these aspects between severe and non-severe COVID-19 cases.

Methods:: A systematic search of PubMed, Scopus and Google Scholar databases was conducted for studies published between the 1st of January 2020 and March 2021. We included all published studies that were English or translated to English, patients from all demographics with a confirmed COVID19 infection (either non-severe or severe) and had sufficiently documented investigation efforts to reach a diagnosis of a neurological manifestations. The main outcomes of the study were to identify the frequency and nature of neurological manifestations and complications, and the neuro-diagnostic findings in COVID-19 patients.

Results:: 389 articles were included with a pooled sample size of 45,340 patients. The mean age was 55 years and 63% were males. The most common neurological manifestations were a combination of minor symptoms such as Myalgia, taste and smell impairment, headache, dizziness and most prominent major manifestations were vascular episodes, encephalopathy, seizures, neuropathies and Gullian Barre Syndrome.

Conclusions:: Neurological involvement is common in COVID-19 patients (whether non-severe or severe). Prompt identification and management of these cases would improve outcome and decrease morbidity.
CRITICAL ILLNESS NEUROPATHY IN SEVERE COVID-19

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Background and Aims:: Neurological complications of COVID-19 have received a growing attention; few studies have described neurophysiological findings in COVID patients during their stay in Intensive Care Units (ICUs). We assessed the presence of either critical illness neuropathy (CIP) or myopathy (CIM) in ICU patients. The mean time of hospitalization in ICU was 17.2 ± 4.1 days.

Methods:: Patients underwent a bilateral examination of the median, ulnar, deep peroneal and tibial motor nerves and of the median, ulnar, radial and sural sensory nerves. F-waves were recorded from abductor hallucis and abductor digiti minimi muscles. Needle electromyography (EMG) was performed for distal and proximal muscles. Direct Muscle Stimulation (DMS) was applied to the deltoid and tibialis anterior; peak to peak amplitudes and onset latencies of the responses evoked by DMS (DMSamp, DMSlat) or by motor nerve stimulation (MNSamp, MNSlat) were compared. The ratio MNSamp to DMSamp (NMR) and the MNSlat to DMSlat difference (NMD) were evaluated.

Results:: Nerve conduction studies showed an axonal neurogenic pattern, with low SAPs and CMAPs amplitudes, as confirmed by needle EMG. MNSamp and NMR were significantly reduced when compared to controls (p < 0.0001), whereas MNSlat and NMD were increased (p = 0.0049; see Figure 1).
Conclusions:: COVID patients suffered from a critical illness neuropathy (CIP), differently from the previous literature showing a higher prevalence of myopathy in non-COVID ICU patients. That could have implications for the functional recovery and rehabilitation strategies of COVID patients, thus delaying ICU discharge, also highlighting novel insights into the neuropathology of COVID-19.
BILATERAL FOOT-DROP SECONDARY TO DEMYELINATING NEUROPATHY POST-COVID-19 INFECTION: A CASE REPORT

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Background and Aims: Covid-19 may cause several neurological symptoms and signs. We present the case of a 27-yo male with bilateral foot-drop after COVID-19.

Methods: A 27-yo male was diagnosed at the end of November 2020 with mild COVID-19. Twenty days later, he presented subacute right hallux paresthesia, extending to the leg and thigh followed by motor impediment in right dorsal foot flexion. In January 2021 similar symptoms involved the contralateral leg and subacute paresthesia developed in the upper limbs. Neurological exam showed steppage gait, conjugate nystagmus in right gaze, hypostenia of the lower and of the right upper limb and severe reduction of the right foot dorsiflexion. Infectious and autoimmune serological work-up was normal; CSF showed IgG 4.2mg/dl (n.v. <3.4) with no oligoclonal bands; Q Alb: 0.62 (n.v.< 0.45). Brain and spinal MRI showed a T2/FLAIR hyperintense lesion at the level of the bulbous-medullary junction. Nerve conduction study/electromyography showed a bilateral neuropathy of the peroneal nerves with segmental demyelination at the level of the fibular head and of the median nerves bilaterally at the level of the carpus. PMP22 gene was investigated, and no mutation was found. Nerve ultrasound did not show any alterations along the course of the peroneal nerves.

Results: Methylprednisolone sodium succinate was administered i.v. (1000 mg/d for five days). The neurological exam after one month showed a partial recovery.

Conclusions: There is a considerable need for studies regarding the potential impact of COVID-19 on the nervous system regarding pathogenesis, prognosis, and severity of disease.
ADEQUATE ACCESS TO MECHANICAL THROMBECTOMY DURING COVID-19 PANDEMIC IN LESSER POLAND VOIVODESHIP IN POLAND

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Background and Aims:: Many studies have shown that COVID-19 pandemic decreased the access to mechanical thrombectomy (MT) in acute ischemic stroke (AIS) patients. We studied, if the pandemic affected the access to MT in Lesser Poland Voivodeship (LPV) located in southeastern Poland (3.36 million of inhabitants).

Methods:: In LPV patients with AIS are admitted to the nearest stroke unit in the region (15-unit Stroke Network), where intravenous thrombolysis is performed. Those fulfilling the criteria for MT are admitted to the Comprehensive Stroke Unit at the University Hospital in Krakow. We compared the number of MT performed within 12 months before pandemic outburst, from March 2019 to February 2020 with the number of MT performed during pandemic, from March 2020 to February 2021. We also compared the time from stroke onset (SO) to groin puncture (GP) during the two studied periods.

Results:: 146 had MTs performed during pre-pandemic period and 182 during the pandemic period. The number of MTs in the consecutive months of both periods was similar up to November. The number of MT doubled from December 2020 to January 2021 as compared to the same period of time a year earlier. The mean SO-GP times were similar in both analyzed periods.
Conclusions:: In LPV the number of MTs during COVID-19 pandemic was similar or even higher as compared to the corresponding pre-pandemic period. The time of the access to MT was not affected by the COVID-19 pandemic. Our results reflect the efficiency of the local medical system for stroke care, irrespectively of the COVID-19 challenges.
COMPARISON OF DISEASE PROFILES AND OUTCOMES OF PATIENTS WITH NEUROLOGICAL DISORDERS WITHOUT AND WITH COVID-19: AN AMBISPECTIVE COHORT STUDY

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Background and Aims:: We aimed at comparing the clinical and laboratory characteristics, along with survival and functional outcome in the form of modified Rankin scale at 3 ± 1 month follow-up, between the COVID-19 negative and positive patients, with a neurological illness.

Methods:: Ambispective cohort study - included patients presenting with a neurological disorder, tested positive for COVID-19, and admitted to the hospital’s COVID-19 centre, from April to September 2020. Demographic, clinical, biochemical and treatment profiles of these patients were compared with COVID-19 negative patients admitted to the neurology wards. Information about three months outcome after discharge was assessed telephonically. Data on survival and disability status in the form of mRS were collected.

Results:: Of a total of 235 patients enrolled from emergency services with neurological disorders, 81 (34.5%) were COVID-19 positive. Mean (SD) age was 49.5 (17.3) years and majority of the patients were male (62.98%). Commonest neurological diagnosis was Acute Ischemic Stroke (AIS)(42.98%). Chronic kidney disease (CKD) patients were more likely to be COVID-19 positive (COVID-19 negative: 4 (2.6%) versus COVID-19 positive: 11 (13.8%), p-value: 0.001). The in-hospital mortality was higher among COVID-19 positive patients (COVID-19 negative: 12 (7.8%) versus COVID-19 positive: 29 (35.8%), p-value: <0.001). There were 15 (13.8%) deaths at three months follow up in the COVID-19 negative versus 4 (12.1%) in COVID-19 positive patients (p-value: 1.00). Overall three-month mRS was higher in the COVID-19 positive group assessed via Cochran-Mantel-Haenszel test (p-value <0.001).

Conclusions:: Patients with neurological disorders presenting with COVID-19 infection had worse outcomes, including in-hospital mortality and three months disability.
Background and Aims:: Recent reviews on the effect of COVID-19 suggest a significant increase in the prevalence of cognitive dysfunction that affects the ability to return to daily functioning. This could be explained by various reasons: (1) Direct neurological damage of Coronaviruses that may penetrate into the brain and cerebrospinal fluid due to increased permeability of the blood-brain barrier or by the infection of peripheral or olfactory neurons. In particular, the hippocampus, a region involved in mnemonic mechanisms, could be a region of great vulnerability; (2) Hypoxia related to respiratory distress syndrome associated with cerebral atrophy and ventricular enlargement and (3) Psychological symptoms manifesting in anxiety, depression or post-traumatic stress syndrome.

Methods:: We propose the analysis of the neuropsychological profile in people infected by SARS-CoV2 and the follow-up at 6 months from the first evaluation. A comprehensive neuropsychological battery was included. Psychological variables (anxiety and depression), verbal and visuospatial memory, attentional functions and processing speed, executive functions and visuospatial functions are explored. Data from medical history and neuroimaging data are collected.

Results:: To date, the main cognitive deficits found are: moderate decreasing in processing speed, impairment of executive functions or difficulties in the information retrieval processes.

Conclusions:: The neurological effect of COVID-19 infection might not be limited to the more well-known symptoms as anosmia or dysgeusia, neuropathies, or exacerbation of pre-existing disease. Cognitive symptoms could be part of the persistent COVID picture and significantly interfere with the work and social activity of those affected. Identifying these symptoms can help us identify therapeutic targets for early neuropsychological rehabilitation.
PROTECTIVE ROLE OF PRE-EXISTING CEREBROVASCULAR DISEASES IN LOCAL SPREAD OF COVID-19 INFECTION IN JAPAN

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Background and Aims:: It is proposed that various pre-existing medical conditions, including cerebrovascular diseases, might increase a risk for severity of coronavirus disease 2019 (COVID-19). The cumulative number of COVID-19 cases in Japan is relatively low, therefore the effect by cerebrovascular diseases can be distinct from that in Western countries. We analyzed the relationship between the local number of patients with pre-existing cerebrovascular diseases per population and local prevalence of patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Methods:: Data on SARS-CoV-2 infection and the estimated number of patients who received medical treatment for cerebrovascular diseases in each prefecture were obtained from the official notifications database of Japan. We analyzed the association between the ratio of patients with each disease and the prevalence of SARS-CoV-2 infection.

Results:: The ratio of patients with cerebrovascular diseases per population showed a significant negative correlation with the prevalence of SARS-CoV-2 infection (Spearman's rank correlation, p<0.01).

Conclusions:: The current study suggests that pre-existing cerebrovascular diseases may play a protective role against local spread of SARS-CoV-2 infection, possibly attributed to common use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers.
THE NEUROLOGICAL PRESENTATIONS ASSOCIATED WITH COVID-19: A RETROSPECTIVE SINGLE-CENTER CLINICAL STUDY IN THE REPUBLIC OF DAGESTAN, RUSSIA

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Background and Aims: Numerous studies have demonstrated that patients with COVID-19 may develop neurological complications, including headaches. Despite this, the available data on the clinical characteristics of affected patients remain limited. The purpose of the study was to analyze the characteristics of headaches in COVID-19 patients examined outpatiendly.

Methods: A retrospective single-center study of the patients with confirmed COVID-19 was conducted from 1st May to 30th June 2020. Epidemiological, demographic, clinical, laboratory and radiological data were collected and analyzed. All patients were divided into 4 groups based on their chest CT scans: CT-0 - no evidence of pneumonia, CT-1<25% involvement, CT-2–25-50%, CT-3–50-75%, CT-4>75%.

Results: 175 COVID-19 patients were enrolled during the study period. The mean age was 49.8±12.3 years (64% females). The leading neurological signs were fatigue (81.2%), headache (64.6%), anosmia/ageusia (54.8%/52.0%), anxiety/depression (58.8%/57.7%). The main features of headache were bilateral localization (72.5%), a pressing quality (69.1%), onset in the frontal and periorbital regions (60.2%) and spontaneous regression after the acute phase of the disease. 57.5% of the patients had no previous history of any primary headache. Headache intensity, according to the VAS, was significantly higher in patients with more severe lung damage (p=0.033), probably due to hypoxia.

Conclusions: Most of the neurological manifestations were comparable in frequency to those reported in the literature. The incidence of headache in our population was higher than reported in the literature, possibly due to the higher rate of primary headache history in our sample of patients compared to available studies.
Background and Aims:: Coronavirus disease (COVID-19), caused by "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2), is characterized by a severe respiratory illness with multisystemic involvement. An increasing number of papers has described electroencephalographic patterns in COVID patients. That is of critical importance not only to corroborate the neuroinvasion sustained by SARS-CoV-2, but also to plan therapeutic strategies, either aggressive or not, for the treatment of seizures. We described four patients with COVID-19 disease, sharing common clinical, EEG and surface electromyographic (poly-EMG) abnormalities.

Methods:: four patients with COVID-19 were enrolled. None of them had a previous history of epilepsy. In each patient, EEG was performed and, in three cases, jerks were also recorded by surface poly-electromyography (poly-EMG).

Results:: Bilateral, symmetric, lateralized periodic discharges (LPD) was recorded in three patients, predominantly in the midline and parasagittal regions. Surface poly-EMG showed synchronous myoclonic jerks, involving the cranial muscles, paralleled by a lack of jerk-locking at EEG-EMG polygraphy, without any correlation between clinical myoclonus and epileptiform discharges and without a proximal-to-distal gradient of appearance.

Conclusions:: This is the first case series of combined EEG and poly-EMG patterns associated to COVID-19 infection, suggesting the presence of a myoclonus of sub-cortical origin, not explained by brain lesions, neither by the hypoxic damage.
Background and Aims:: COVID-19 is a rapidly emerging respiratory disease caused by SARS-CoV-2. Numerous studies have demonstrated that patients with COVID-19 may develop neurological complications. Despite this, the available data on the clinical characteristics of affected patients remain limited. The purpose of the study was to present the clinical manifestations and predictors of severe outcome of COVID-19 patients examined outpatiently at the Diagnostic Center of the Republic of Dagestan, Russia.

Methods:: A retrospective single-center study of the 175 patients with confirmed COVID-19 was conducted from 1st May 2020 to 30th June 2020. Epidemiological, demographic, clinical, laboratory and radiological data were collected and analyzed. All patients were divided into 4 groups based on their chest CT scans: CT-0 - no evidence of pneumonia, CT-1 <25% involvement, CT-2 – 25 to 50%, CT-3 – 50 to 75%, CT-4 > 75% involvement.

Results:: 175 COVID-19 patients were enrolled during the study period. The mean age was 49.8±12.3 years. Female was the dominant sex (64%). The leading neurological signs were fatigue (81.2%), headache (64.6%), anosmia/ageusia (54.8%/52.0%), anxiety/depression (58.8%/57.7%). A comparative analysis revealed no significant differences in the prevalence of neurological symptoms in patients with different severity of lung involvement. Older age, female sex and comorbidity – obesity, arterial hypertension and diabetes mellitus were estimated as higher risk factors for severe form.

Conclusions:: The first Russian retrospective study of COVID-19 adult patients was presented. There were no patients in our cohort with a new-onset neurologic event. The main neurological manifestations were comparable in frequency to those reported in the literature.
NEURON SPECIFIC ENOLASE IN A SARS COV2 PATIENT

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Background and Aims:: Neuron-specific enolase (NSE) is a dimeric, intracellular, glycolytic enzyme, which is released after stroke, cardiac arrest, traumatic brain injury. Serial assessment of its level may help in identification of patients at risk of poor outcomes, in decision making on intensive care, rehabilitation or palliative treatments.

Methods:: An 80 years-old male patient came to our observation for confusion. At past case history, chronic coronary syndrome in aortic-coronary by-pass, mild-moderate mitral failure, paroxysmal atrial fibrillation, pulmonary emphysema, type II diabetes mellitus, recent SARS CoV2 were reported.

Results:: Level of NSE was high (30,8 ng/ml). Episodes of O2 saturation below 90%, decreased lymphocyte absolute counts and g globulins were still present. IgM and IgG titers and nasopharyngeal swab were negative. Electroencephalogram showed dysrhythmia, with diffuse slow waves. Chronic cerebrovascular disease was evident at neuroimaging.

Conclusions:: Our observations confirm our previous finding on worst outcomes after CoV2 infection in immunodepressed patients with comorbidities. We highlight that NSE may be a useful marker to assess the clinical course in anoxic encephalopathy. However, it is dependent on the ratio between neuronal and glial cells. Low levels do not rule out ongoing damage. In elderly patients, S100, a calcium-binding, astroglial protein may be more consistent. On the other hand, the brief half-life of the latter (25 minutes) compared to the longer half-life of former marker (30 hours) may limit detection. Both may implement clinical and radiological findings, especially in ventilated and sedated patients. Lastly, they may add further information for ethical, social and legal issues.
NICOTINE, CYTOKINE STORMS AND COVID-19

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Background and Aims:: The association of smoking with chronic obstructive pulmonary disease and cardiovascular disease puts smokers at increased risk of complications of COVID-19. Counterintuitively perhaps, several reports have found reduced prevalence of current smokers among patients admitted to hospital with COVID-19, suggesting a protective effect of active smoking against severe COVID-19.

Methods:: We report on an frail elderly man with a longstanding history of bipolar affective disorder associated with heavy smoking, alcohol dependence and multiple medical co-morbidities, including chronic obstructive airways disease and recurrent pulmonary sepsis, who contracted COVID-19 during his inpatient stay for treatment of a manic episode.

Results:: Against expectations and despite multiple risk factors for severe COVID-19, he fully recovered without the need treatment or respiratory support.

Conclusions:: We discuss the potential impact of his substantial use of nicotine replacement therapy during his inpatient stay on the eventual outcome of his illness. Nicotine, an α7-nACh receptor agonist, may boost the cholinergic anti-inflammatory pathway and hinder the uncontrolled overproduction of pro-inflammatory cytokines triggered by the SARS-CoV-2 virus, which is understood to be the main pathway to poor outcomes and death in severe COVID-19. While further research is required, evidence of a protective effect of nicotine against complications of COVID-19, although still speculative, would be strong argument for ensuring smokers are routinely provided adequate nicotine replacement on admission to hospital. More importantly, it would be yet another reason to persuade smokers to switch to nicotine replacement therapy, and ultimately quit.
SELF-REPORTED OLFACTORY DYSFUNCTION IN MEXICAN HEALTHCARE WORKERS DURING THE FIRST SIX MONTHS OF THE COVID-19 PANDEMIC: A NATIONWIDE ONLINE SURVEY STUDY

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Background and Aims:: After the first reports of olfactory dysfunction (OD) in the context of COVID-19, a rise of OD was described in different countries. Therefore, the Mexican Academy of Medicine, in conjunction with the National Institute of Neurology and the School of Medicine (UNAM), launched last April a nationwide online survey to describe the frequency and characteristics of self-reported OD in self-identified healthcare workers (HCWs) from Mexico.

Methods:: This 45-question instrument was based on the one previously reported by Bagheri et al. Non-probability sampling was used. The survey was distributed through official social media and institutional mailing lists. Only HCWs were included in this analysis.

Results:: Among 2702 responders, 1295 (47.9%) HCWs (784 women) completed the survey (median age 32 years). 126 (9.7%) HCWs reported OD in the last month. Of these HCWs with OD, 76 (60.3%) were previously healthy. Fever and/or chills before or during OD were reported by 43 (34.1%) HCWs. 75 (59.5%) HCWs reported respiratory symptoms before OD. In the last month, 61 (48.4%) HCWs also reported any kind of gustatory dysfunction. 57 (45.2%) HCWs reported having treated patients with COVID-19. Of them, 28 (22.2%) were diagnosed with COVID-19, but only 3 reported having been hospitalized due to COVID-19. In total, 35 of all the HCWs who completed the survey were diagnosed with COVID-19, and 80% reported OD in the last month.

Conclusions:: In this survey, less than 10% of Mexican HCWs reported OD during the first six months of the COVID-19 pandemic.
GIULIAN BARRÉ- MILLER FISHER SYNDROME RELAPSE DURING SARS-COV2 INFECTION- A CASE REPORT

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Background and Aims:: Miller Fisher Syndrome (MFS) is an uncommon variant of the spectrum of Guillain Barré Syndrome (GBS). MFS relapses are rare and often described after long asymptomatic intervals. GBS-MFS spectrum has been reported in association with SARS-COV2 infection. We present a SARS-COV2 associated GBS-MFS relapse.

Methods:: We detail patient's characteristics and compare with previous reports.

Results:: A 60-year-old man, diagnosed with GBS-MFS in March 2020, was admitted at Emergency Department in February 2021 with incomplete asymmetric ophthalmoplegia, ataxia, areflexia, four limbs weakness and paraesthesia and mild bifrontal oppressive headache. CSF analysis was unremarkable. Nerve conduction studies on day 7 showed a motor demyelinating polyneuropathy. Serum anti-GQ1b IgG antibodies were negative. Molecular SARS-COV2 test was positive although he was asymptomatic, except for mild fever three days after onset, at the same time with neurological symptoms worsening. Blood tests revealed mild leukopenia and CRP elevation. He was treated with intravenous low dose dexamethasone, subcutaneous enoxaparin for 10 days and with intravenous immunoglobulins for 5 days. Neurological symptoms resolved after 20 days, concurrently nasopharyngeal swab tested negative. Compared to previous reported SARS-COV2 associated GBS-MFS, in our case neurological symptoms came first, with para-infectious rather than post-infectious immune mediated mechanism. Latency of not SARS-COV2 triggered relapses was longer (median 7 years) with usually positive anti-GQ1b IgG antibodies.

Conclusions:: To the best of our knowledge, this is the first GBS-MFS recurrence description during SARS-COV2 infection. Its underlying immune mechanism seems to differ from SARS-COV2 related monophasic reports, with shorter latency and probably different antibody profile than not-SARS-COV2 linked relapses.
RACE AND SEX DIFFERENCES IN COVID-19 VACCINATION HESITANCY AMONGST PATIENTS WITH NEUROLOGICAL DISORDERS IN HAWAII

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Background and Aims:: This quality improvement (QI) project was conducted in order to better understand how demographic factors may influence the likelihood of COVID-19 vaccination hesitancy and declination in patients with neurological disorders in Hawaii.

Methods:: Adult patients who had visited Hawaii Pacific Neuroscience (HPN) between January 1, 2019 to January 1, 2021 were contacted through a telephone QI survey to assess COVID-19 vaccination hesitancy in relation to patient race and sex. Over 30 different sociodemographic variables and medical comorbidities were examined. Statistical analysis utilized univariate and multivariable logistic regression to determine variables associated with vaccine acceptance.

Results:: Amongst all sex and race strata, odds of COVID-19 vaccine acceptance were significantly lower for those perceiving the vaccine as unsafe. After multivariable logistic modeling, the strongest predictors of vaccine hesitancy were identified. For females, predictors included concerns of vaccine safety (p=0.0094) and the self-perception of a pre-existing medical condition contraindicating vaccination (p=0.00050). Amongst males, predictors included not receiving the flu vaccine within the past year (p=0.037), perception that COVID-19 is not a severe illness (p=0.037), and being politically conservative (p=0.034). For Whites, predictors included concerns of vaccine safety (p=0.044) and a high school education only (p=0.037). Amongst Asians, predictors included concerns of vaccine safety (p=0.0066) and the self-perception of a pre-existing medical condition contraindicating vaccination (p=0.014). For Native Hawaiians/Pacific Islanders, the only predictor was a positive depression screening (p=0.040).

Conclusions:: Patients with neurological disorders exhibit different predictors for vaccine hesitancy, dependent upon race and sex. Hence, tailoring vaccine education per race and sex may increase outreach effectiveness.
POSTCOVID-19 NEUROLOGICAL SYNDROME: A PROSPECTIVE STUDY AT 3600 METERS ABOVE SEA LEVEL IN LA PAZ BOLIVIA

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Background and Aims:: Background. COVID-19 is the newest, most publicized, widely read, best known and controversial infectious disease. There are few publications on post-covid neurological complications in patients who attend neurological outpatient consultation. We present a case report of the population of La Paz, Bolivia, elevation 3600 meters above sea level.

Methods:: Methods. A prospective study was conducted from March 2020 to March 2021. Medical records of 5070 patients who attended outpatient neurological consultation were analyzed. We describe the new-onset neurological manifestations of 237 consecutive patients with laboratory-confirmed SARS-CoV-2 infection and submit a review of their medical histories by a neurologist.

Results:: Results. Of these 5070 neurological patients, 3280 were women (64.7%) and 1790 were men (35.3%); 237 of these patients presented post-covid neurological manifestations (4.67%). 151 were women (2.97%), 86 were men (1.69%). 41% had CNS involvement (headache, vertigo, seizure, memory disorders, tremor), 57% had PNS involvement (paresthesia, weakness, painful polyneuropathy, trigeminal neuralgia), 45% musculoskeletal involvement (myalgia, polyarthralgia) and 35% neuropsychiatric compromise (anxiety, depression, insomnia). The majority (78%) presented 2 to 4 symptoms.

Conclusions:: Conclusions. The "post-covid neurological syndrome" represents a diagnostic challenge for the clinical neurologist due to the multiple manifestations: central and peripheral nervous system, musculoskeletal and neuropsychiatric symptoms, without structuring a classic semiology, intense and constant headache, insomnia, anxiety and unexplained depression in patients without prior history. The response to classic treatment is variable, since the symptoms can be varied and wide-ranging (resembling a moth bite). We are just beginning to learn about this complex, novel and highly infectious disease.
EXACERBATION OF SYRINGOMYELIA/SYRINGOBULBIA SYMPTOMS AFTER COVID-19: CASE REPORT

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Background and Aims: In syringomyelia there is a known Substance P (SP) overexpression, predominantly in the external laminae of the dorsal horn. It has been hypothesized that several infections, particularly COVID-19, may increase the expression of the TRPV1 gene in lung, producing an increment of SP and IL-6, which would involve an alteration of the spinal trigeminal nuclei responsible for its secretion. The aim is to report the first case of exacerbation of syringomyelia/syringobulbia symptoms after a COVID-19 infection.

Methods: A 42-year-old Hispanic female patient with history of syringomyelia/syringobulbia with Chiari malformation treated with decompressive surgery in 2019, presented to clinic in June 2020 complaining of close to 8 months of pain in the left upper limb, after suffering COVID-19 infection in August. One month later, the pain increased exacerbated by exertion, along with cold allodynia and tinnitus. Physical examination showed hypertension, anomic aphasia, cold allodynia with left hemitremor; dysesthesias, pain and weakness in left upper limb; lower limbs hyperreflexia; and bilateral Hoffman and Marinescu. Bloodwork showed elevated ESR and CRP. SARS-CoV-2 IgM and IgG were positive. MRI showed Chiari Malformation and syringomyelia/syringobulbia.

Results: The patient received COVID-19 treatment improving all features. Anecdotally when corticosteroids were weaned off pain returned; imposing a new corticosteroid regimen after which pain subsided returning to her daily living activities.

Conclusions: This is the first case report of an exacerbation of syringomyelia/syringobulbia symptoms after COVID-19. We propose substance P as a key mediator for this kind of features.
Background and Aims:: SARS-CoV-2 induces an immunological response that can trigger encephalitis and several movement disorders like chorea, opsoclonus, myoclonus, tremor and ataxia. SARS-CoV-2 receptor protein ACE-2 is expressed in the brain and its gene is closely related to the dopamine decarboxylase gene, which catalyzes the conversion of L-DOPA into dopamine which can be altered in COVID-19. The aim is to report a case of COVID-19 presenting with choreiform movement disorder as the core neurological complication.

Methods:: A 86-year-old hispanic male with COVID-19 presented with persistent nocturnal dyspnea, buccopharyngeal dystonia, dysarthria, night sweats, dry mouth, generalized pruritus, insomnia, headache and involuntary movements. Followed by sialorrhea with dysphagia and dystusia. Physical examination showed hypoacusia, tangential thinking, frontal release signs, facial and upper limbs choreiform movements with lip smacking, tongue biting, facial, upper limbs weakness and lower limbs paresthesias, diminished deep tendon reflexes and Romberg’s. Bloodwork showed elevated glucose, ESR, CRP, CPK, ferritin, fibrinogen and D-dimer. SARS-CoV-2 IgM and IgG were positive. MRI showed fronto-parietal subcortical ischemic lesions, as well as at the centrum semiovale, and faint hyperintensity of the claustrum and the rostral putamen.

Results:: The patient received treatment for COVID-19 with corticosteroids, and overcame the infection. Involuntary choreiform movements disappeared improving the rest of his symptoms.

Conclusions:: Chorea movement disorders should be taken into account as a neurological complication of SARS-CoV-2 infection as we report in this case.
DAILY CHRONIC HEADACHE DUE TO GIANT CELL ARTERITIS POST COVID-19: CASE REPORT

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Background and Aims:: Anxiety disorders, migraine, and vasculitides, such as Giant Cell Arteritis (GCA), may occur following several viral infections, including SARS-CoV-2 and they present an emerging challenge for clinical neurologists in the current COVID-19 pandemic. Its mechanisms include endothelial cell inflammation, apoptosis and dysfunction. We report a case of chronic headache due to GCA accompanied by anxiety disorder and probable inflammatory bowel disease following COVID-19 infection. The aim is to report a case of a daily chronic headache due to GCA accompanied by anxiety disorder following COVID-19 infection.

Methods:: A 44-year-old Hispanic female who denied previous history of COVID-19 presented with persistent, intense, dull-oppressive, occipital-temporal, crown-like irradiation headache accompanied by mouth-face weakness, and amaurosis-like visual disturbances. Other symptoms included anxiety attacks, insomnia, stress and hearing discomfort. Anxious behavior and mood changes persisted with oppressive chest pain, nausea and vomiting. Physical examination showed tachycardia, jaw claudication, pain in occipital and right temporal region and at the temporal artery, tinnitus, bilateral cervical trigger points, positive Marinescu and Romberg’s. Bloodwork showed negative ESR and CRP, positive ANA 1/160 and elevated calprotectin. SARS-CoV-2 IgM was positive. Doppler ultrasound of the right temporal artery showed a positive halo sign, thus giant cell arteritis diagnosis was established, and regular treatment was initiated.

Results:: The patient underwent partial resolution of the symptoms after receiving corticosteroids, paroxetine, propanol, topiramate, and a gluten-free diet.

Conclusions:: Autoimmune diseases, like giant cell arteritis, could appear in patients with an unknown or asymptomatic history of COVID-19. SARS-COV2 infection should be considered as a trigger of postinfectious vasculitides.
STATUS EPILEPTICUS AND COVID-19: A SYSTEMATIC REVIEW

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Background and Aims:: Among the symptoms included in the SARS-CoV-2 infection-related coronavirus Disease (COVID-19), neurological manifestations have been frequently reported. In this systematic review, we summarized the available data on clinical features, diagnosis, and therapy of COVID-19-related Status Epilepticus (SE)

Methods:: We performed a systematic search of the literature to identify data on demographics, clinical, neurophysiological, and neuroradiological data of patients with COVID-19 related-SE. The following electronic databases and data sources were systematically searched: MEDLINE (accessed through PubMed), EMBASE, and Google Scholar (from December 2019 to January 2021). In all databases we used the following search strategy: ("epileptic state" OR "epileptic state") AND ("coronavirus disease 2019" OR "coronavirus disease 2019"). We included all studies reporting cases of SE in the context of COVID-19 syndrome in patients with or without a previous history of epilepsy, published in English, and reporting individual patient data. Non-peer reviewed papers were excluded. We used regression models (linear or logistic) with a stepwise forward method to identify features associated with mortality or severity of SE.

Results:: Thirty-nine articles were included with a total of 47 cases of SE associated with COVID-19. Age, time between the acute respiratory phase of SARS-CoV-2 infection and SE onset, and hospitalization correlated with a higher SE severity as assessed by quantitative validated scales.

Conclusions:: SE can be a neurological manifestation of SARS-CoV-2 infection. Although a possible association between SE and COVID-19 has been reported, the exact mechanisms are still not fully understood. Systemic inflammatory syndrome due to cytokine release could play a role in COVID-19 related SE.
Impact of COVID-19 Pandemic on Incidence of Health-Care Associated Infections in Neurology Intensive Care Unit (ICU) and Its Associated Mortality – A Retrospective Cohort Study

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Background and Aims: Health care-associated infections (HCAI) are leading cause of mortality in Intensive Care Unit (ICU). The coronavirus disease 2019 (COVID-19) pandemic has led to mandatory use of masks and personal protective equipment (PPEs) in addition to standard infection control practices. This may additionally lead to benefit in the decrease of HCAI besides decreased risk of transmission of COVID-19. Aim: To compare the incidence of HCAIs and in-hospital mortality among patients admitted in the neurology ICU during the COVID-19 pandemic period and pre-pandemic period.

Methods: In a retrospective cohort study design, patients admitted to the Neurology ICU during the initial five months of the Covid-19 pandemic period (1st April – 31st August 2020) and the same calendar months of the prior year in the pre-pandemic (1st April – 31st August 2019) period were included. The prevalence of HCAIs and in-hospital mortality in these groups was compared.

Results: Forty-seven patients in the pandemic period and 52 patients in the pre-pandemic period were admitted in the Neurology ICU during the study period. The prevalence of HCAI was 72.3% in the pandemic period and 69.2% in the pre-pandemic period (p value: 0.73). The median person days of antibiotics during the pandemic period was 49 (31-71) days as compared to 60.5 (25-110) days during the pre-pandemic period (p value: 0.41). The mortality during the pandemic and pre-pandemic period was 27.6% and 40.4% respectively (p value: 0.18).

Conclusions: The augmentation of infection control practices prevented the spread of Covid-19 but could not provide additional improvement in HCAI prevention.
NEUROLOGICAL COMPLICATIONS OF COVID-19: A MONOCENTRIC EXPERIENCE OF A NEUROLOGICAL OUTPATIENT CLINIC

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Background and Aims:: Since the onset of the COVID-19 pandemic, numerous central and peripheral nervous system complications related to the virus have been observed. Here we present a case series of neurological complications from our outpatient clinic dedicated to patients with previous SARS-CoV-2 infection.

Methods:: We set up a “Neuro-COVID Outpatient Clinic” in November 2020 for the management of patients referred by the Pneumology Unit of our Hospital and who complained of neurological symptoms.

Results:: Up to the date (April 2021) from a total number of 319 patients who referred to the Pneumology Clinic, we have collected data from 62 patients (31 female) with a mean age of 59 years (18 – 80 years). Of these, 53 patients were previously admitted to our ICU or to the Pneumology Department. The most frequent complications (27) were those related to peripheral nervous system including plexopathies, critical ill neuropathies, and isolated cranial nerve palsies. Six patients developed previously unreported headache and 5 dizziness, while 16 patients complained of memory impairment. A patient developed symptoms of Myasthenia Gravis with anti-AchR antibodies. We observed two cases of myoclonus and cerebellar ataxia. An 18-year-old patient suffered of ischemic stroke in the absence of other risk factors. Twenty-two patients developed anosmia, and 8 of these still present anosmia after 6 months from the infection.

Conclusions:: Neurological complications related to SARS-CoV-2 infection are far from rare. Some of these are to be referred to the long hospitalization but others could be the consequence of parainfectious or postinfectious mechanisms.
PERSISTENT AURA-LIKE VISUAL PHENOMENON AS THE UNIQUE MANIFESTATION OF COVID-19 POST-INFECTIOUS WHITE MATTER LESION: A CASE REPORT.

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Background and Aims:: A visual aura lasting longer than 1 week is defined as persistent. Cortical spreading depression (CSD), a propagating wave of neuronal depolarization, followed by long lasting suppression of cortical activity, is the electrophysiological phenomenon thought to underlie migraine visual aura. Disorders which alter the state of neuronal excitability may increase brain’s susceptibility to CSD by lowering the threshold for neuronal depolarization.

Methods:: A 29-year-old woman was admitted to our department reporting subacute onset, three weeks before, of persistent vision of shining, colored lights in right visual hemifield. Two weeks before the onset of symptoms she was diagnosed with asymptomatic COVID-19. Medical history was remarkable for migraine with aura.

Results:: Neurological examination and blood tests were unremarkable. Computerized campimetry showed decreased retinal sensitivity in right visual hemifield. Brain and spinal cord MRI showed a unique, round, post-contrast enhancing lesion in left peritrigonal white matter (involving left optic radiation). CSF analysis showed type3 oligoclonal bands (evidence of systemic and intrathecal immune activation). EEG showed left temporo-occipital (sometimes generalized) sharp waves. Neither a trial with diazepam nor a treatment with IV methylprednisolone were effective on visual symptoms. She started lamotrigine (100mg/daily) with progressive improvement of symptoms.

Conclusions:: This case showed how an acquired structural abnormality, such as an inflammatory post-infectious white matter lesion, can alter the state of neuronal excitability and increase brain’s susceptibility to cortical depolarization, thus manifesting with positive symptoms, i.e. an aura-like persistent phenomenon. Hence, any change in aura pattern and frequency, even in migraineurs, requires exclusion of secondary forms.
Background and Aims:: Describe the neuropsychiatric symptoms in 300 patients requiring hospitalization surviving at the largest COVID-19 care center 3 months after discharge.

Methods:: An exhaustive neurological evaluation was performed on 300 patients 3 months after hospital discharge following COVID-19 at the national institute of respiratory diseases in Mexico City, a COVID-only institution for the time being. All patients underwent a neurological symptom survey, complete neurological examination, cognitive evaluation with MoCA and MMSE screening tests, and some laboratory tests, by 2 expert neurologists. The patients were stratified as follows: mild COVID those who only required the use of nasal prongs during hospitalization, moderate COVID those who required high oxygen flows with the use of a reservoir mask, high-flow nasal prongs, and severe COVID those who required advanced management of the airway during hospitalization.

Results:: The mean age was 58 years +/- 13 years, 69% of the patients were male, 15% were health personnel. No comorbidity was statistically significant between groups. The main manifestations are hyposmia, dysgeusia, dizziness, vertigo, headache, myopathic pain, affective symptoms, insomnia, cognitive complaint, and arthralgias, with a statistically significant difference in sensorimotor neuropathy and neuropathic tremor in severe patients. Mean MoCA scores in mild patients were 27 while in moderate and severe patients 25 points. MMSE scores were 28 in mild patients, 27 in moderate to severe patients.

Conclusions:: Adequate follow-up of post-covid patients is needed for symptomatic surveillance and to prevent long-term sequelae.
Background and Aims:: Subjects with Myasthenia Gravis (MG) could be at risk for severe complications with Coronavirus Disease (COVID-19), even though few data are available. The aim of the present study is to describe the clinical characteristics and outcomes in patients with MG and COVID-19 and identify clinical factors associated with COVID-19 severity and risk of hospitalization, requirement of respiratory support and death.

Methods:: We retrospectively analyzed demographic variables and clinical characteristics of 63 MG patients (F 47.6%; M 52.4%, mean age 53 ± 16 y) who were diagnosed with COVID-19 based on a PCR test from a nasopharyngeal swab and/or SARS-CoV-2 serology. Main outcomes were the need of hospitalization, the requirement of respiratory support and death for COVID-19.

Results:: Overall 5 patients deceased for Covid infection (7.9%). As in general population, older age (p <0.001) and hypertension were independently associated with hospitalization, whilst obesity (p 0.022) was associated with poorer outcome disregarding hospitalization. Only Myasthenia Gravis Foundation of America (MGFA) class was correlated with worst outcome (p 0.010). Interestingly no correlation was found between immunosuppressant treatment at baseline and severity and outcome of infection.

Conclusions:: Most MG patients in this study fully recovered from Covid-19 and experienced milder forms of infection. Neuromuscular disease was well controlled, at most with increasing steroid dose briefly. Independent risk factors correlated with severity disease and poor outcome were similar to general population. Patients with highest MGFA class have an additional risk for severe disease course and deserve special attention.
Background and Aims:: Since the outbreak of COVID-19 that is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 2020 throughout the world, a lot of aspects of people’s lives are affected including their psychological status. Follow-up assessment of survivors of this infection showed that they had multiple psychological disorders including depression, panic attacks, obsessive compulsive disorder, and post-traumatic stress disorder.

Methods:: A Narrative Review of Mechanisms

Results:: It is estimated that more than one-third of patients with COVID-19 experience neuropsychiatric symptoms, including headache, paresthesia, and disturbed consciousness. Among patients affected by COVID-19, there are different mechanisms that can cause cognitive dysfunction. COVID-19 can affect the central nervous system (CNS) directly by invasion and indirectly by inducing hypoxia, inflammation, and delirium. The pandemic and fear of infection can also cause anxiety which impairs the cognition as well.

Conclusions:: By assessing the patients’ cognition and knowing the higher probable cause of cognitive impairment, we can form a better strategy to better treat the impairment. Cognitive behavioral therapy can be effective in reducing the anxiety and cognitive rehabilitation therapy (CRT) can be used to lower the detrimental effects of cognitive impairment caused by COVID-19.
Background and Aims:: During SARS-CoV-2 pandemic people with multiple sclerosis (PwMS) may experience a worsening due to increased anxiety and depression, reduction in rehabilitation, and less strict connection to MS centres. The aim of our study was to describe the self-reported impact of SARS-CoV-2 pandemic and lockdown on PwMS.

Methods:: On June 2020, we enrolled PwMS who underwent teleconsult during the lockdown phase (March-May 2020). Self-rated worries for pandemic, perception of change in anxiety, depression, fatigue and spasticity was asked, as well as changes in weight, physical activity and food intake. We compared patients with and without reported increase in: spasticity, anxiety, depression and fatigue. Binary logistic regression analyses were applied including significant variables. Statistical significance was set at p<0.05.

Results:: Ninety-three MS patients were enrolled (71% female, 77% RR, median age 50.3y, mean disease duration ≈13y). Many patients reported an increase of anxiety (36.6%), depression (34.4%), fatigue (26.9%) and, spasticity (18.3%), weight (47.3%) and 63.4% of patients reported reduction of physical activity; moreover 59.1% and 43% reported particular worries for the pandemic and the perception of greater impact on PwMS of the pandemic compared to general population, respectively. In the multivariate models, anxiety was predicted by depression, particular worries for SARS-CoV2 pandemic and reduction in physical activity; depression by anxiety; fatigue by reduction in physical activity; spasticity by EDSS.

Conclusions:: The self-reported impact of pandemic on PwMS was deep in terms of increased depression, anxiety, fatigue and spasticity, mainly related to reduction in physical activity and pre-existing disability.
Background and Aims:: Telemedicine in multiple sclerosis (MS) is promising, particularly for patients with high disability and difficulties to reach the treating centre. During SARS-CoV2 pandemic, teleconsults are gaining a central role. The aim of the present study was to report our single-center experience and to verify the effectiveness of teleconsults in diagnosing relapses and rating progression.

Methods:: During the first lockdown phase (March-May 2020) all the pre-planned consults were converted in teleconsults. The evaluation focused on new symptoms or worsening of known symptoms, disability (PDDS), patients' satisfaction of such assessment modality (rated form 0 to 10). Patients were then re-evaluated in person within 6 months. We verified the changes in disability and the accuracy of teleconsults in diagnosing MS relapses.

Results:: Eighty-four patients underwent teleconsult and were re-evaluated in person within 6 months after the lockdown (69% female, mean age 50.5±11.0y, mean disease duration 13.0±9.7y 78.6% relapsing-remitting disease form, 76.2% on disease modifying treatment). Median pre-lockdown EDSS was 1.5 (range 0-8) median EDSS post lockdown was 2 (1-8) (p=0.836); median PDDS during lockdown was 1.5 (0-8). A single disease relapse was detected with teleconsults. In the post lock-down in person evaluation no additional undiagnosed relapses were detected. Patients' reported satisfaction was very high (median 10, range 8-10).

Conclusions:: Teleconsult in MS patients allowed us to guarantee a regular neurological follow-up during pandemic lockdown. No unreported relapses were missed, no significant disability changes were reported nor detected compared to pre-lockdown evaluation. Finally, patients' satisfaction of this modality was very high.
THE OUTBREAK OF METHANOL INTOXICATION DURING COVID-19 PANDEMIC: PREVALENCE OF BRAIN LESIONS AND ITS PREDISPOSING FACTORS

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Background and Aims:: During the COVID-19 pandemic, methanol-containing beverages’ consumption has risen because people mistakenly believed that alcohol might protect them against the virus. This study aimed to evaluate the prevalence and predisposing factors of brain lesions in patients with methanol toxicity and its outcome.

Methods:: A total of 516 patients with confirmed methanol poisoning were enrolled in this retrospective study, of which 40 patients underwent spiral brain computed tomography (CT) scan.

Results:: The presence of unilateral or bilateral brain necrosis was significantly higher in the non-survival group (p = 0.001). Also, intracerebral hemorrhage (ICH) and brain edema were prevalent among patients that subsequently died (p = 0.004 and p = 0.002, respectively). Lower Glasgow Coma Scale (GCS) was related to a higher mortality rate (p = 0.001). The mortality rate in chronic alcohol consumption was lower than the patients who drank alcohol for the first time (p = 0.014).

Conclusions:: increasing the number of methanol poisoning and its associated mortality and morbidity should be considered a threat during the COVID-19 pandemic.
THE PROBABILITY OF NEUROCOGNITIVE DISORDERS IN PATIENTS AT THE POSTCOVID STAGE

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Background and Aims:: Актуальность постковидных расстройств у больных обусловлена отсутствием данных о механизмах возникновения нейрокогнитивных расстройств.

Methods:: Material and methods of research. We examined 22 people who had suffered from COVID-19, which made up two groups. The first main group – 10 patients with clinical signs of mild cognitive impairment (LCN), the second comparative group – 12 patients without clinical signs of LCN. To detect LCN, neuropsychological tests MMSE were used, tests were performed: "establishing patterns", visual-spatial function, semantic mediation and generalization. In the comparative analysis, the nonparametric criterion χ2 was used, based on the null hypothesis that there are no differences between the compared groups.

Results:: The results obtained. If in group 2 there was a positive dynamics of cognitive functions of patients in the form of a statistically significant (p<0.05) increase in the number of correctly completed tasks on the MMSE test on average 27.9 ± 1.3, D= 10.3%; p < 0.05, "+" 2.6 points, then in group 1 there was no positive dynamics (p<0.05). In group 2, there is an increase in words called in one repetition, averaging 1.3 words (20.3%), while in group 1 patients there is a negative trend (p<0.05). In the "digit repetition test", the increase in the total score of reproduced digits both in the forward order (+2.2 points, 5.0% in contrast to the patients of group 1) and in the reverse order (+3.2 points, 8.5% in contrast to group 1) was significant (p<0.05). The "Complex figure" revealed a significant (p<0.05) decrease in the time spent on the task in patients of group 2 (-6.3 seconds; 10.5% compared to group 1; p<0.05).

Conclusions:: Thus, Covid-19 causes LCN in patients in at least 50% of cases.
IMPACT ON AIR POLLUTION IN DELHI AND INCIDENCE OF STROKE IN LIEU OF COVID-19 LOCKDOWN

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Background and Aims:: Exposure to air pollution is now well recognized by scientists, media and the population as a major public health issue. The Delhi air flux is the most pernicious consequences of indiscriminate industrialisation and urbanisation. The significant improvement in the air quality of Delhi region was observed due to strict implementation of lockdown. During the lockdown period, improvement in ambient air quality helped us in circumventing the coronavirus community spread.

Methods:: Cross Sectional Study was designed. All strokes within 2-weeks from onset & within one year of event were screened & recruited. PM2.5 was measured in areas of Delhi in using the help of DCPCB. Incidence of recurrent stroke was assessed during the covid-19 lockdown period. Stroke severity was calculated on the basis of NIHSS, mRS scale.

Results:: 50 patients recruited. Out of them 6 patients had recurrent stroke (min-3 & Max-6) in last one year. The mean age for patients was 52.3±11.2 years with a mean NIHSS of 5.86±1.3 and mean mRS of 1.04±0.07. The higher level of PM 2.5 was 230 and minimum was 65 during the Covid-19 Lockdown period i.e March-May-2020. We found that the higher level of PM 2.5 is associated with incidence of Stroke. Maximum six recurrent attack reported by single patient when PM2.5 level was ≥650 from October2019-January2020. 2 patients with history of severe RHD reported recurrent attack during the lockdown period.

Conclusions:: Increased level of air pollution particles matter effects on brain and increased the recurrent incidence of stroke. PM2.5 decreased during the lockdown period and less recurrent stroke reported at same time.
Background and Aims:: The present pandemic caused by the Novel Coronavirus 2 (SARS-CoV-2) is predominantly but not restricted to respiratory illness. Neurological complications in the acute phase have been well characterized like Encephalopathy, psychosis, stroke but there is paucity of data about post covid presentations. We aim to study the various neurological syndromes seen in Covid19 patients following discharge.

Methods:: From July 2020 to December 2020, 1150 Laboratory confirmed Covid 19 cases were admitted and treated in a tertiary care hospital. Patients who developed Neurological syndromes after discharge and within 6 weeks were studied.

Results:: During the follow-up period, A total of 1150 Covid 19 positive patients treated in the IP department. Out of these 10 patients with severe ARDS requiring ventilator died, one patient died of MI, 5 people bedridden at discharge. Among the survivors a total of 19 (1.6%) Patients presented with neurological complaints within 6 weeks of discharge. Of these Ischemic Stroke-2, Hemorrhagic Stroke-1, ADEM-1, Optic neuritis – 2, Epilepsy -1, GB syndrome -1, Persistent Headache -2, Bell’s Palsy-1, Sensorineuronal deafness – 2, Severe fatigue -3, Myalgias -2, Severe vertigo -1. There were 12 Male and 7 Female, age ranged from 40 yrs to 65yrs (Median -54yrs), Co-mobidities: Diabetes – 12, Hypertension – 7.

Conclusions:: SARS- CoV2 infection can cause neurological complications in both acute phase as well as in the follow up period. The pathophysiology need to be studied to plan for the management and prevention of these disabling neurological syndromes.
PATHOMORPHOLOGICAL CHANGES OF THE BRAIN IN PATIENTS WITH COVID-19

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Background and Aims:: COVID-19 is a global disease and was characterized as a pandemic by the WHO and the coronavirus is caused also damage nervous system. The aim of this study was to investigate the brain tissue of patients who died from COVID-19.

Methods:: We investigated the brains of 15 patients who died from complications of COVID-19. All patients had a positive test for SARS-CoV-2. Information from the autopsy protocol included macroscopic and microscopic characteristics of brain and general autopsy findings. We used immunohistochemistry staining for astrocytes, microglia and T-lymphocytes in the cortex, basal ganglia, brainstem and cerebellum.

Results:: All patients died in hospitals and had a median age of 65 years (range, 47–80 years), 66,7% male and 33,3% women. Cause of death of most cases was viral pneumonia as the underlying condition. Neuromorphological studies showed fresh ischemic infarction in three (20%) patients with focal encephalolysis. Hypoxic manifestations with neuronal loss in the frontal lobe, basal ganglia, hippocampus, cerebellum were present. In most of cases the arteriolosclerosis with perivascular rarefaction was present. The reactive astrogliosis with positive astrocytic marker GFAP was seen in all cases but showed variable degrees. The perivascular activation of microglia and the microglial nodules with CD68 positive cells were in the cortex, basal ganglia, hippocampus, brainstem, but less in cerebellum. And perivascular infiltration by CD3 was most pronounced in the brainstem.

Conclusions:: Thus, the morphological changes of the CNS associated with Covid-19 include ischemic infarction with encephalolysis, astrogliosis, microgliosis, perivascular infiltration by CD3 in different regions of the brain.
MUSCLE MANIFESTATIONS AND CK LEVELS IN COVID INFECTION: RESULTS OF A LARGE COHORT OF PATIENTS INSIDE A PANDEMIC COVID-19 AREA

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Background and Aims:: Objective: to investigate both muscular manifestations and CK levels in a large cohort of patients with COVID-19 infection and to determine whether hyperckemia is associated with morbidity and mortality.

Methods:: Data of 615 patients discharged from ASST Ovest Milanese (Milan, Lombardy, Italy) with final diagnosis of COVID-19 infection were retrospectively extracted from electronical medical records from 21 February to 1 May 2020. Patients were descriptively analyzed with respect to the following variables: sex, age, muscular manifestations (myalgia and/or arthralgia), fatigue, respiratory involvement (SARS pneumonia or respiratory failure) and history of falls. Association between patients’ characteristics and CK levels was investigated. In addition, the proportion of patients who died following access to the ER was calculated. Finally, the effect of CK levels and other patients’ features on mortality was estimated using a logistic regression model.

Results:: 176 (28.6%) patients had raised serum CK levels. CK levels were significantly associated with history of falls, male gender, SARS pneumonia, respiratory failure and in-hospital death. No correlation was found between hyperckemia and muscular manifestations.

Conclusions:: Our study provides preliminary evidence that hyperckemia is associated with respiratory failure and fatal outcome in patients with COVID-19 infection. In these patients, among other testing, CK dosage is recommended.
ASYMPTOMATIC PERIPHERAL NEUROPATHY IN PATIENTS WITH SARS-COV-2 INFECTION

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Background and Aims:: Several neurological complications related to SARS-CoV-2 infection have been reported. The involvement of peripheral nervous system (PNS) consists in the development of immune-mediated neuropathies such as Guillain-Barré Syndrome. In this study we aim at assessing the presence of asymptomatic abnormalities in peripheral nerves conduction during the acute phase of COVID19 and, their correlation with blood circulating inflammatory markers.

Methods:: Thirty-nine patients with COVID19 were assessed by electroneurographic study of lower limbs and blood tests within one week of hospital admission (T0) and after 30±10 days (T1).

Results:: Electroneurographic changes were found at least on one nerve at T0 in 12 patients, consisting of axonal or demyelinating changes. Two biological markers were found to be significantly correlated with the presence of neuropathic changes: Reactive Protein C and lymphocyte count. Patients with pathological electrophysiology at T0 showed significant improvement of electrophysiological parameters at T1. The improvements in electroneurographic data were significantly correlated with the trend of laboratory parameters, in particular with fibrinogen, D-Dimer, ferritin, C Reactive protein and lymphocytes. None of the patients with neuropathic changes developed clinical evidence of a full-blown peripheral neuropathy over time.

Conclusions:: Our study shows that asymptomatic alterations of the PNS can be found during the acute phase of COVID19. These alterations significantly improve after 20-40 days from the acute phase of infection and that the improvement correlates significantly with the trend of laboratory parameters. Further studies are needed to evaluate possible long-term neurological complications and the predictive value of subclinical damage of PNS in the acute phase of infection.
NEUROCovid: Can CSF immune reactivity give new insight on neurological manifestations in COVID-19 patients?

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Background and Aims:: Neurological manifestations have been increasingly associated with COVID-19, but there is little evidence of a direct viral pathogenesis. Clinical heterogeneity and confounding factors also impair the search for alternative mechanisms. Therefore, we studied the CSF of 13 patients with neurological symptoms during the acute phase of their hospitalization, looking for clues suggesting a specific dysimmune phenomenon.

Methods:: CSF underwent conventional analysis and RT-PCR for SARS-CoV-2; a in-house HEK293 cell-based assay was also arranged to identify anti-spoke antibodies. Albumin ratio, IgG index and oligoclonal bands were also assessed, along with a screening for autoimmune antibodies. First, commercial immunofluorescence and lineblot were used to detect common neuronal surface and intracellular antibodies, respectively; secondly, immunohistochemistry was performed on rat brain sections; lastly, CSF was incubated with fixed murine neuron and astrocyte cultures to confirm a potential auto-reactivity.

Results:: CSF analysis disclosed a slightly increased protein level with a non-significant cell count (0-10 cells/μL). Neither SARS-CoV-2 nor common neuronal antibodies were detectable in the CSF, but we recognized anti-spoke IgGs. 69% of the samples also showed neuropil staining, some of which had a common staining pattern involving the hippocampal dentate gyrus. Rodent primary cultures confirmed the presence of autoreactive antibodies against epitopes that are expressed in cortical neurons and/or astrocytes in most samples.

Conclusions:: A strong immunoreactivity against spike protein was found in the CSF of those patients, even without a significant blood brain barrier permeability. The detection of autoreactivity with two different techniques could thus represent a dysimmune response to COVID-19 infection, perhaps suggesting molecular mimicry.
PAEDIATRIC TRANSVERSE MYELITIS DURING COVID-19 ASYMPTOMATIC INFECTION: A CASE REPORT

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Background and Aims:: Paediatric Transverse myelitis (TM) is a rare, demyelinating immune-mediated disorder of the Central Nervous System. Its immunopathogenesis is not completely understood. Viral infections are recognised triggers that precede TM in 66% of cases. Although uncommon, neurological involvement with spinal cord damage can occur following SARS-CoV2 infection. Although the co-occurrence of TM and SARS-CoV2 is more frequently observed in adults, children may also be affected.

Methods:: We report a paediatric case of TM during SARS-CoV2 asymptomatic infection.

Results:: A 12-year-old boy complained of severe nuchal pain that lasted for a few hours and was followed by hyposthenia on the right hemisoma persisting for approximately 12 hours. Brain MRI scan was normal. Spinal cord MRI demonstrated a T2/FLAIR hyperintense lesion, enhancing post-contrast, at C2 level. CSF and blood microbiology and virology were negative. CSF SARS-CoV2 genoma sequencing and oligoclonal bands were negative. Serology for AQP4 and anti-MOG antibodies was negative. Acyclovir, azithromycin and high dose intravenous methylprednisone were also administered for 8 days. The patient completely recovered and was discharged after 11 days with steroid tapering. He had a follow-up spinal cord MRI a month later that returned normal.
Conclusions: Neurological complications during SARS CoV2 infection are rare in children, but may occur as a consequence of dysimmunity possibly triggered by SARS CoV2.
THE FIRST YEAR OF NEUROLOGY AND COVID 19: THE IMPORTANCE OF UNDERSTANDING NEUROLOGICAL AND BIOPSYCHOSOCIAL SYMPTOMS IN ACUTE AND POST NEUROCOVID DISEASE

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Background and Aims:: After the first year since its first reporting Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing Coronavirus disease 2019 (COVID-19), has infected nearly 120 million people and resulted in almost more than 2 million deaths globally. After one year from the first report of neurological symptoms in a Chinese patient, more than 55 countries to date have reported symptoms including impaired taste or smell, headache, dizziness, delirium, agitation, stroke, hypoxic ischaemic brain injury, seizures, coma, meningo-encephalitis, Guillain-Barré syndrome, myalgia, amongst others. Consequences seen in the follow-up periods of COVID-19 infection are also becoming more and more apparent mostly with reports of persistent problems with smell or taste, cognitive impairment, headaches, confusion, difficulty concentrating and sleep disturbance

Methods:: Recently more and more studies on long term consequences of acute Covid are being published, such as the Study NEXT, a longitudinal study done in a population of hospitalized patients in Brescia

Results:: first studies show that not only clinical but also biopsychosocial effects are becoming increasingly important as long as more data are collected

Conclusions:: Although further research is needed to understand which patients are most vulnerable to neurological manifestations in the acute, long or post COVID-19 disease, however after this first year it is clear that neurological, biopsychosocial and mental health data need to be not only collected but also analysed in a manner that could help the understanding of characteristics, timing, and severity of neurological manifestations of COVID-19.
BELL’S PALSY FOLLOWING POST COVID-19 INFECTION MYOCARDITIS IN PREGNANCY: THE FIRST CASE REPORT

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Background and Aims:: Lower motor neurone facial nerve palsies are a rare complication of SARS-CoV-2 infection. Bell’s palsy following COVID myocarditis has been reported previously but whether they are associated is not known. We report the first case of the above combination in pregnancy.

Methods:: A 27-year-old Sri Lankan in her 2nd pregnancy complicated with pregnancy induced hypertension since POA of 26 weeks presented at 30 weeks with fever, productive cough and exertional dyspnoea for 4 days. She was tachypnoeic (RR - 40/min) and tachycardic (PR – 120/min). There was a left-sided mild pleural effusion (later confirmed by ultrasound) with clear lung fields. (SpO₂ - 97%). The ECG had widespread T inversions and ST-depressions, 2D-Echo had global hypokinesia with a thin rim of pericardial fluid. Serum troponins were marginally elevated (0.4ng/ml). She had a neutrophil leucocytosis with elevated ESR (120mm/1st hour), CRP(291mg/l) and D-dimers (1249ng/ml). Deep vein thrombosis and pulmonary embolism were excluded by imaging. Blood and urine cultures were negative. The SARS-COV-2 PCR was weakly positive with a strong positivity for COVID antibodies. Serology for enterovirus, rickettsia, Legionella and Mycoplasma were negative. She had an uneventful recovery after a hospital stay of 2 weeks managed symptomatically and with prophylactic antibiotics.

Results:: One-week post-discharge she presented a left sided Bell’s palsy without other neurological signs, symptoms; a phenomenon reported by many. She was treated with Galvanic stimulation and oral steroids for 10 days and made an uneventful recovery in 2 weeks.

Conclusions:: COVID in pregnancy is a predisposition to Bell’s palsy. It’s association with myocarditis should be sought.
COVID-19: THE NATURE OF PAIN IN COMPLICATIONS OF THE MAXILLOFACIAL REGION.

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Background and Aims:: Patients with coronavirus disease have severe complications in the form of thrombosis, facial bone necrosis. Purpose: monitoring of the nature of pain syndrome in maxillofacial region of patients with Covid-19

Methods:: Clinical analysis was carried out in 50 patients who applied to the TMA clinic. The average age of patients was 60 ± 9.0 years, including 27 women (54%) and 23 men (46%), with diagnosis of cavernous sinus thrombosis, osteomyelitis of jaw 1–3 months after the onset of acute Covid-19 disease. During the 10-day period of hospitalization and 6 months of rehabilitation, the pain was assessed according to a 10-point criterion (pain load - 0 points, very strong - 10 points) through the questionnaire.

Results:: N. Facialis paresis was in 39 patients, paresthesia of the 3rd corneal nerve in 28 patients. Local pain was observed in 15% of the head, 50% irradiated to facial nerve and 35% in the area of facial inflammation. After the first 10 days of treatment, pain decreased from 10 to 2.5 points in 35% of patients. Severe pain was observed in 10% of patients (8-10 points), and in 25% of patients, the average simultaneous pain in the local jaw area remained within 3.5 ± 0.38 (p≥0.05). In 15% of patients, the headache persisted up to 4-5 (on average) points, in 15% of patients the headache completely disappeared. The mean pain score was 2.6 ± 0.3 (p ≥ 0.05) in all patients older than 6 months.

Conclusions:: In patients undergoing COVID 19, with thrombosis, facial necrosis severe pain persisted long time.
Background and Aims:: The research team decided to investigate: Structure, etiology, and features of the course of epilepsy syndrome in patients admitted to hospital with suspected or confirmed coronavirus infection and concomitant and/or concomitant diagnosis of epilepsy syndrome (call an ambulance for development of seizure\ seize in presence of emergency doctor)


Results:: 12% (7) reported a fatal outcome (seizures in acute stroke period\ epilepsy+severe covid-19// symptomatic epilepsy - metastases in brain + covid-19)
In 81% (46), covid-19 was successfully treated. In 7% (4), a transfer to another specialized hospital.
1. Patients are unable to report whether they have had previous epilepsy episodes - 17.6% (10);
2. An epilepsy episode developed for the first time - 33.3% (19)
3. Epilepsy episodes have been reported before - 49.1% (28).

According to the etiology of the epilepsy syndrome (on classification 1):
1. The background of acute neurological disorder (cerebral edema: acute stroke period// newly detected large brain mass) – 7%(0-4-0)
2. The background of exogenous intoxication by alcohol and psychoactive substances - 25.5% (6-4-11);
3. Unclear etiology - 19.3% (4-7-0);
4. Poststroke seizure – 12.3% (0-3-4);
5. Idiopathic epilepsy – 8.8% (0-0-5);
6. Symptomatic epilepsy (the background of brain masses) – 8.8% (0-0-5); 7. In the structure of other diseases - 5.3% (0-0-3).

Conclusions:: -Frequency of admission “covid-19 + epilepsy syndrome” less in comparison over the same period;
-The etiology of exogenous intoxication still predominates; -The mortality in the cohort is not higher than in other groups.
UNUSUAL BRAIN MRI FINDING IN A PATIENT WITH COVID-INDUCED PERSISTENT CACOSMIA

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Background and Aims:: Olfactory dysfunction is emerging as a key symptom of COVID-19 along with other neurological complications. Herein we describe a case of persistent cacosmia with an unusual finding on brain MRI.

Methods:: In March 2020, a 50-year-old woman with no relevant medical history developed fever, dry cough, diffuse muscle pain, sudden onset of anosmia and ageusia. She was diagnosed with Covid-19 by positive result on PCR analysis. Her clinical course was uncomplicated. Anosmia and ageusia started improving after two months. However, during the recovery phase she started perceiving distorted and unpleasant smells in response to stimuli (cacosmia) as well as sudden unpleasant smell sensations without any odorant stimuli (phantosmia). These symptoms persisted for 9 months, therefore she was referred to our neurology clinic.

Results:: Neurological objective examination was normal. EEG with olfactory stimulation showed a normal pattern. Brain MRI was performed after 10 months from the onset of symptoms. 3D FLAIR images showed an evident cortical hyperintensity in the medial olfactory stria and in the adjoining cortex of the subcallosal gyrus (Figure 1 – 2).
Conclusions:: This report shows an unprecedented signal alteration on MRI in a patient with persistent cacosmia and phantosmia 10 months after Sars-Cov2 infection, reinforcing the hypothesis of Sars-Cov2 neurotropic propagation through the olfactory system.
A POST COVID-19 GUILLAIN-BARRE SYNDROME

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**Background and Aims::** Guillain-Barré syndrome consists of clinical syndromes that manifest as an acute or subacute autoimmune inflammatory polyradiculoneuropathy with resultant weakness and diminished reflexes. It is also part of so-called Yuki syndrome. Its annual incidence is 1-2/100000. The exact cause of Guillain-Barre syndrome is unknown. But two-thirds of patients report symptoms of an infection in the six weeks preceding. These include respiratory or gastrointestinal infection (EBV, C.jejunii) or Zika virus. Smaller studies have suggested a link between COVID-19 and GBS. But when researchers compared the number of GBS cases recorded in the UK's National Health Service database in 2016 to 2019 to the number recorded in the first half of 2020, they found the annual incidence was 40% to 50% lower during the pandemic.

**Methods::** The patient had physical examination, imaging, blood tests.

**Results::** A 66 old man was admitted in the hospital 20 days after COVID-19 infection with complaints of paraesthesias and weakness in the legs, low back pain and feeling of incomplete miction, lasting for 5 days. The examination revealed also areflexia in the legs. Later complaints in the hands were added. CSF showed 1 g/l protein and normal cells. The diagnosis GBS was settled after EMG and CSF examination and proper treatment was started with good outcome.

**Conclusions::** The relation between COVID-19 and GBS is far from any prove, but its absence is still controversial. There are number of cases of GBS after COVID-19 infection, but this still can be only coincidence.
Background and Aims:: We describe the headache pattern during the acute stage of COVID-19 as well as the headache after discharge at 3 months of hospitalization in 400 in an exclusive COVID-19 care center in Mexico City.

Methods:: A complete neurological assessment was performed 3 months after discharge, obtaining the type of headache, pattern, duration and intensity of the headache as well as the presence of previous headache. Data on persistent headache after COVID-19 or after hospital discharge were also obtained for 400 patients with positive PCR for SARS-CoV-2.

Results:: Of the 400 patients evaluated, 49.3% had recent onset headache. The distribution of pain was Holocranial (42.6%), Hemicranial (11.5%), Bifrontal (31.1%), Occipital (14.8%), Bitemporal (23.0%). The type of pain was Oppressive (63.3%), Pulsatile (21.7%), Stabbing (18.3%). With a duration of less than 7 days (25.0%), 1-2 weeks (31.7%), less than 1 month (6.7%), 1 month to 3 months (8.3%), still have it (28.3%), 71% of the patients had moderate to severe headache. Less than 7% had headache prior to COVID-19 of these 50% had migraine. 38.7% presented post COVID headache, 66% still presented headache at 3 months, of Holocranial localization (33.3%) and bitemporal 25% oppressive in 62% and mild to moderate.

Conclusions:: Post COVID-19 headache is very prevalent and can be very disabling. Recognizing and treating this sequela is very important as it can improve the quality of life for survivors of this pandemic.
NEUROLOGICAL COMPLICATIONS OF COVID-19: A TUNISIAN SERIES

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Background and Aims:: A number of neurological disorders have been reported to be associated with the novel corona virus: COVID-19 (acute or post) including acute stroke, encephalitis, convulsions, peripheral neuropathy and rarely myelitis.

Methods:: It’s a retrospective study carried out at the neurology department of Fatouma Bouguiba Monastir hospital including patients who had SARS-CoV-2 infection with neurological complications, between September 2020 and February 2021.

Results:: We included 7 patients, the middle age was 58.14 years and the sex ratio is 2.5. A viral RNA PCR from a nasal swab was performed in 6 patients who returned positive and a chest CT scan was done in a single case showing sequel of Covid-19. The time from COVID-19 symptoms to neurological symptoms was between 5 days and 3 weeks. Central nervous system involvement was found in 5 patients: 4 cases had an ischemic stroke; these patients were older, had cardiovascular comorbidities (arterial hypertension, diabetes mellitus and obesity) and had more severe respiratory impairment. A case of acute transverse myelitis has been reported in which we did not detect SARS RNA in the CSF. The case of myelitis is among the rarest reported cases worldwide. Peripheral nervous system involvement was found in 2 patients. The outcome was good in all patients.

Conclusions:: Neurologic complications associated with SARS-CoV-2 infection are polymorphic. It is important to recognize potential neurologic manifestations and complications of the noval corona virus especially when some of which can be rapidly progressing and require urgent intervention.
LACK OF CONCENTRATION AND ITS CORRELATION WITH COVID-19 IN MEDICINE ACADEMICS.

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Background and Aims:: The emergence of COVID-19 and its global expansion, put the world into an emergency and unprecedented scenario. Social detachment seems to be the most effective preventive form so far, and this has led to significant changes in medical education and human behavior. This work aims to evaluate the concentration of medical school students and its relation with the social and psychological changes during the COVID-19 pandemic.

Methods:: Online questionnaire was answered on the Google Forms by 153 volunteer medical students from the Municipal University of São Caetano do Sul. The students are from first to fifth year of medical school. Written approval was granted.

Results:: A question was asked: Did you have difficulty concentrating during the quarantine? The answers were: 5,2% said YES, 64,7% had difficulties in many moments, 8,5% said NO and 21,6% had difficulties in rare moments.

Conclusions:: In such a delicate moment as the current one, the great stress generated in medical students, caused important changes in mood and social behavior, culminating in a difficulty in concentrating in most of the interviewees.
THE INFLUENCE OF COVID 19 ON MEDICAL STUDENTS MEMORIES

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Background and Aims:: A pandemia de Covid 19 trouxe muitas mudanças na vida de muitas pessoas, incluindo estudantes de medicina. Por ser uma situação inesperada, muitas pessoas têm seus estilos de vida, estudos e empregos afetados. Portanto, este trabalho tem como objetivo analisar como a memória de estudantes de medicina foi afetada durante uma pandemia.

Methods:: Um questionário online foi aplicado a 153 estudantes de medicina que foram voluntários, entre eles, alunos do primeiro ao quinto ano. Obtivemos aprovação por escrito. Os alunos responderam à pergunta: Você teve alguma alteração de memória durante a quarentena?

Results:: The percentages of the answers was: 49.7% of the volunteers replied that their memory is the same. 34.6% answered that they have some memory difficulty. 9.8% said that the memory is a little better. 4.6% replied that their memory is severely impaired e 1.3% replied that the memory is much better.

Conclusions:: A maioria relatou nenhuma mudança na memória, e outra grande parte relatou dificuldade de memória. No entanto, também houve um número considerável de melhorias relatadas. Isso mostra que apesar de ser um momento estressante para todos por causa da pandemia, o processo de formação da memória é individual e afetado pelo ambiente subjetivo de cada um.
MILD COVID-19 INFECTION ASSOCIATES WITH PERSISTENT NEUROLOGICAL SYMPTOMS

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Background and Aims:: Little is known about post-covid-19 neurological symptoms. We aimed to assess neurological manifestations of post-COVID-19 patients and their relation to severity.

Methods:: We performed a cross-sectional analysis of 779 consecutive COVID-19 patients (PCR-confirmed) in the post-acute stage (585 women, median age 42, median interval post-infection 48 days). All participants filled the form (https://forms.gle/vgoyHQ6wftkucgtM8). We performed a multinomial logistic regression with cross-entropy optimization to predict subject cluster using sex, treatment modality (outpatient (696), non-ICU inpatient (52) and ICU inpatient (31)) and age groups as regressors. SciPy 1.5.2 and Scikit-Learn 0.23.2 Python packages were used for the analyses.

Results:: Most of the participants were polysymptomatic (18.6% were asymptomatic, 19.6% had one symptom, 17.1% had two symptoms, and 44.7% presented three or more symptoms), including fatigue (48%), headache (34%) and memory problems (29.8%). Cluster analysis divided the 779 individuals into five clusters of subjects (anosmia predominant, oligosymptomatic, polysymptomatic, headache predominant and fatigue/memory predominant), and four clusters of symptoms (headache, fatigue/memory issues, anosmia/ageusia and miscellaneous symptoms). Regarding treatment, the non-ICU inpatients (compared to the outpatients) were less likely to be in the anosmia-predominant cluster (p=0.04); the ICU inpatients (compared to the outpatients) had a higher probability of being in the fatigue-memory cluster (p=0.001). Women presented a higher chance to be in the headache cluster (p<0.001) and a lesser chance to be in the oligosymptomatic (p<0.001) and fatigue-memory predominant (p=0.02) groups.

Conclusions:: Anosmia seems associated with milder manifestations, and the fatigue-memory group appears associated with ICU admission. Women presented more headache and were more polysymptomatic than men.
SEVERE NEUROLOGICAL MANIFESTATIONS OF PATIENTS INFECTED WITH THE SARS-COV-2: REGISTRY IN INTENSIVE CARE UNIT.

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Background and Aims:: Introduction The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been associated with many neurological manifestations, mainly encephalitis, meningitis, acute cerebrovascular disease (ischemic and hemorrhagic), Guillain Barré syndrome (GBS) and seizures. Background In late December 2019 a novel coronavirus was identified in China causing severe respiratory disease. The virus causing the infection has been named - severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Symptoms are mainly respiratory, around 40% may manifest with mild neurological symptoms.

Methods:: Methods We included 35 patients with SARS-CoV2 infection hospitalized in Intensive Care Unit, with presentation of severe neurological events.

Results:: Results Our hospital (San José, Tecnológico de Monterrey) has treated 2,920 patients infected by COVID19 in 1 year, 351 patients have required intubation, 1.19% have severe neurological manifestations and the reported mortality is 11.4%. This cohort includes 82% males, median age 57.9 (+/- 14.96 years), first day of consultation by the neurology service was 22.21 (+/- 19.8 days), most frequent neurological presentation was encephalitis in 31.4%. The rest of neurological events were 5.7% myasthenic crisis, 2.9% microangiopathy, 5.7% guillain barre syndrome, 11.4 % status epilepticus, 22.9% STROKE, and around 20% presented Posterior reversible encephalopathy syndrome (PRES) and Autonomic dysfunction in ‘long COVID’.

Conclusions:: Conclusion Reports of severe neurological involvement in COVID-19 are increasing, which makes this problem particularly relevant to neurological critical care therapy. The nervous system can be directly or, more frequently, indirectly be involved. We anticipate that these neurological events will represent a large proportion of primary and secondary care consultations in coming months.
Background and Aims:: Fatigue and “brain fog” are frequently complained by patients even after mild COVID-19. We investigated whether these symptoms could be related to central neurological dysfunctions.

Methods:: Sixty-seven patients complaining of fatigue and/or “brain fog” and 22 healthy subjects (HS) were enrolled. Fatigue, perceived exertion (evaluated after motor task) and “brain fog” were evaluated. Global cognition and executive functions were assessed with Montreal Cognitive Assessment (MoCA) and Frontal Assessment Battery (FAB). Attention was measured with Sustained Attention, Stroop and Navon computerized-tasks. Transcranial magnetic stimulation (TMS) of the primary motor cortex (M1) evaluated resting motor threshold (RMT), motor evoked potential (MEP) amplitude, and cortical silent period (SP). Intracortical activity was evaluated with paired-pulse TMS protocols including short-interval intracortical inhibition (SICI), reflecting GABA_A-mediated inhibition, long-interval intracortical inhibition (LICI), a marker of GABA_B receptor activity, and short-latency afferent inhibition (SAI) that indexes central cholinergic transmission.

Results:: Patients reported high level of perceived fatigue, exertion and “brain fog”. MOCA and FAB highlighted poorer performances in patients than HS. At computerized tasks, both, sustained and executive attention were impaired. Patients presented higher RMTs, lower MEPs amplitude and longer SPs, as compared to HS, concurring with a reduced M1 excitability. LICI and SAI were impaired, indicating altered GABA_B- and cholinergic neurotransmission.

Conclusions:: Overall, our results demonstrate, in long COVID-19, an important link between fatigue, “brain fog” and central nervous system dysfunctions, characterized by frontal lobe cognitive impairments and altered neurotransmission.
DIFFERENTIAL CHARACTERISTICS IN THE MANAGEMENT OF ACUTE CONFUSIONAL SYNDROME SECONDARY TO COVID-19 PNEUMONIA.

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Background and Aims:: Acute Confusional Syndrome (ACS) is the most common neuropsychiatric complication in COVID-19 infection. Its management is still a challenge because the data and recommendations based on the evidence are limited. To describe the differential characteristics of the hospital management of ACS in patients with COVID-19 pneumonia compared to ACS secondary to other causes.

Methods:: An observational descriptive study has been carried out in patients with ACS who have required assessment by the liaison psychiatry service of Hospital del Mar between February to April 2020. The sample was divided in 2 groups (with and without COVID-19 pneumonia). Chi-square and Fisher's tests were used for comparisons.

Results:: The total sample was 62 patients, 26 of them diagnosed with COVID-19 pneumonia. The duration of ACS was longer in COVID-19 patients, mean of 12.68 days (SD 13.64). Dexmetomidine (26 vs 0) and olanzapine (13 vs 3) were used more frequently in COVID-19 patients, p<0.001. In COVID-19 patients a greater number of different antipsychotic drugs were used, mean of 2.40 (SD 1.323), and they received less family support (4) compared to non-COVID-19 (22), p <0.005.

Conclusions:: ACS associated with COVID-19 pneumonia in the patients in our sample is more difficult to manage than ACS associated with other pathologies, similar to which described in other series. It is related to a longer duration of the confusional symptoms and difficulties for control it.
MORPHOLOGICAL CHANGES IN THE SPINAL CORD TISSUE IN PATIENTS WITH GUILLAIN-BARRÉ SYNDROME ASSOCIATED WITH COVID-19.

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Background and Aims:: Коронавирус может преодолевать гематоэнцефалический барьер (ГЭБ) и проявлять нейроинвазивные свойства. Точные механизмы проникновения в центральную нервную систему еще полностью не изучены, но сейчас предполагается четыре пути передачи. Первый из них - обонятельные нервы. Второй путь проникновения вируса в центральную нервную систему - клеточная инвазия. В этом случае моноциты и макрофаги, инфицированные коронавирусом, проникают через ГЭБ и опосредуют нейроинвазию. Эндотелиальные клетки BBB - третий возможный путь нейроинвазии; они способны экспрессировать два типа рецепторов - ACE2 и CD209L. Четвертый возможный путь проникновения вируса в нервную систему - это трансинаптическая передача через периферические нервы. Objective: To study morphological changes in the spinal cord in Guillain-Barré syndrome in patients with COVID-19

Methods:: Autopsy material from 3 patients with confirmed Guillain-Barré syndrome due to COVID-19.

Results:: Histological examination of the spinal cord material revealed that the structure of the nuclei is sharply disturbed, large foci of neuronal loss up to complete devastation, single preserved neurons, numerous shadow cells, pronounced edema, sharp depression of the neuropil, axonal degeneration, amyloid bodies.

Conclusions:: SARS-CoV-2 can damage spinal cord tissue, causing severe damage and death. Perhaps the virus is able to persist in the form of inactive fragments for a long time, the disease can recur in susceptible individuals when appropriate conditions arise.
COGNITIVE FOLLOW-UP IN COVID-19 RELATED ENCEPHALOPATHY TREATED WITH IMMUNOGLOBULINS

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Background and Aims:: Covid-19 can manifest through a pletora of neurological manifestations1, among which of particular interest is Covid-19-related encephalopathy (CRE)2. Treatment with intravenous immunoglobulins (IVIG) has been proposed3 but no study is currently available for long-term follow-up.

Methods:: We evaluated 3 CRE patients 6 months after infection resolution. Two patients had a comprehensive neuropsychological assessment, while the third underwent a phone interview.

Results:: All our patients had normal brain MRI, diffuse slowing of EEG tracings and also aspecific cerebro-spinal fluid results. The first patient, a 55-year-old female who had a confusional state, soon after the IVIG course scored 23.2 on the Mini Mental State Examination (MMSE). At follow-up, MMSE was 27.3 but the patient had deficits in memory and fluency and complained of sleep disturbance. Patient 2, a 76 year-old male who also presented with confusion, had 21.7 on MMSE after IVIG. At 6 month-repeat evaluation, his MMSE was 27.2 but deficits in frontal functions were present. The third patient, a 70 year-old female already diagnosed with dementia, had a baseline MMSE of 19, and during Covid-19 presented akinetic mutism. At follow-up she was back to her previous status, but she complained about severe insomnia.

Conclusions:: All patients showed a remarkable positive effect after IVIG, nonetheless they reported various long-term sequelae: the 2 patients who could be tested had both cognitive deficits, and 2 patients out of 3 reported sleep difficulties. These data need confirmation by follow up cognitive studies in further cases.
Background and Aims:: To prospectively assess neurological manifestations in patients with confirmed COVID-19 requiring hospitalization, and to analyze them according to the clinical outcome.

Methods:: At hospital admission, neurological examination was performed on 105 patients (aged 57. ±13 years; 31 women), with an evolution time of 9.8 ±3.5 days and no history of neurological disease, but t2 diabetes (36%), high blood pressure (36%) and overweight/obesity (81%), After follow-up until discharge, comparisons between survivors/deceased patients were performed using “t” test.

Results:: At admission; the SOFA score was 0-16 (median 3) and 21 (20%) patients required immediate respiratory support with sedation (RASS -2--5, median -5; Glasgow 3- 15, median 3); at the end of follow-up 60 (57.8%) patients died. Somatosensory and cerebellar dysfunctions were infrequent, while mental dysfunction (particularly acalculia) was frequent; 22 patients (21%) had delirium and 7 (6%) showed pyramidal signs. Anecdotic report of anosmia and dysgeusia was more frequent in surviving than in deceased patients (75% versus 53% & 50% versus 36%, p >0.05); however, evaluation of the first cranial nerve (excluding sedated patients) showed more frequent impairment in those who died than in survivors (28% versus 9%); cranial nerve impairment decreased during the first 3 days of hospitalization (dexametasone was administered to all the patients). Neurological manifestations were more frequent in patients with diabetes (p<0.05), in whom persistent hyperglycemia and thrombocytopenia were observed.

Conclusions:: In patients with late hospitalization due to COVID-19, neurological manifestations may be more frequent in those with diabetes and might be related to a negative outcome.
YOUNG WOMAN WITH PERSISTENT HEADACHE A WEEK AFTER COVID-19 VACCINATION - 
REPEATED INVESTIGATION IS CRUCIAL

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Background and Aims:: Cases of cerebral venous sinus thrombosis (CVST) with concomitant 
thrombocytopenia were reported in young women following administration of COVID-19 Vaccine 
AstraZeneca (AZD1222/ChAdOx1-S). CVST is a rare but potentially fatal event, to be included in the 
differential diagnosis of headaches.

Methods:: Case report of a previously healthy, 18-year-old, female soldier who presented with NSAID-
resistant frontal headache and remittent nausea in our casualty department 7 and 9 days after her first 
AZD1222-vaccination. No-smoker, no intake of oral contraceptives or other drugs reported.

Results:: First visit, day 7 post vaccination: Neurological examination and laboratory results were 
unremarkable, except for elevated D-dimers (4.12mg/l [<.55]) and CRP (.6mg/dl [<.5]). Platelets: 150/nl
[150-450]. SARS-CoV2-IgG: negative. Dual-energy CE-CCT/CTA revealed no CVST or other pathological 
findings. The patient was discharged. Second visit, day 9 post vaccination: Persisting headache. No focal 
deficit, no petechiae. Thrombocytopenia (55/nl). D-dimers 15.29mg/l, CRP 1.1mg/dl. CCT now showed 
clear CVST (superior sagittal/transverse/sigmoid sinuses). Admitted to our Stroke Unit, treatment started 
with fondaparinux and immunoglobulins (PF4-heparinELISA-positive vaccine-induced 
thrombotic thrombocytopenia, VITT). Seizures were treated with levetiracetam. Because of progressing CVST and 
additional parenchymal bleeding we performed endovascular mechanical thrombectomy. Recanalisation 
was achieved. Platelet-count normalized. Patient recovered.

Conclusions:: Persisting headache after application of COVID-19 vector-based vaccines should be 
taken seriously even in healthy young women with no apparent vascular risk factors, initially normal 
platelet-count and unremarkable cerebral imaging. Reevaluation with repeated investigation 
(examination/laboratory/imaging), if neurologic symptoms persist, might be crucial to detect suspected 
CVST. Early and extensive therapy with IVIG and endovascular mechanical thrombectomy needs further 
evaluation in these cases.
A CASE OF GUILLAIN-BARRÉ SYNDROME AFTER COVID-19 VACCINATION

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Background and Aims:: ChAdOx1-S (Vaxzevria, formerly known as AstraZeneca) is an adenoviral vector vaccine against coronavirus disease 2019 (Covid-19). To date, a number of side effects have been reported in association to this vaccine, in particular thrombosis.

Methods:: Review of the patient’s medical history.

Results:: We describe a case of Guillain-Barré Syndrome (GBS) after administration of a single dose of ChAdOx1-S in a 57-year-old man, with no history of other plausible risk factors for this neurological condition. Clinical presentation was consistent with the GBS variant known as bifacial weakness with paraesthesias; diagnosis was confirmed by neurophysiological and cerebrospinal fluid (CSF) findings. During hospitalization, blood tests showed electrolytic alterations suggestive of syndrome of inappropriate secretion of antidiuretic hormone (SIADH). According to published guidelines, our patient promptly received a course of intravenous immunoglobulins (2 g/Kg over 5 days), without any complications and gradual clinical improvement. To our knowledge, this is the first report of GBS associated to ChAdOx1-S vaccine. Given the importance of monitoring adverse drug reactions after commercialization, this case was reported to AIFA (Agenzia Italiana del Farmaco) via online procedure.

Conclusions:: The spectrum of effects due to Covid-19 vaccines has to be deeply investigated.
IMPACT OF COVID-19 PANDEMIA ON THE CARE OF PATIENTS WITH SPINAL CORD INJURIES (SCI): AND ITALIAN SURVEY.

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Background and Aims:: To assess how Covid-19 impacted the clinical practice specialized SCI units.
Methods:: Survey circulated to the personnel of specialized SCI centers in Italy.
Results:: Two hundred people answered the survey. Most of them (63%) reported that during the last year there has been a reduction of the number of new SCI and a reduction of the number of beds available for patients with SCI. In 68% of the centers patients with SCI and Covid were admitted, but mostly (47%) after a negative swab. In all units Covid screening is regularly performed. Almost all the visit of relatives to the patients were suspended. Despite all these precautions, 52% of the respondents reported that some patients were found positive during their stay in the unit. Most of them (58%) (depending on the clinical situation) were transferred to Covid units. 95% of the respondents reported that the precautions adopted against the virus changed working modalities, halting some aspects of the clinical practice (e.g. outdoors activities, formal meetings with the relatives, caregivers training, evaluation of architectural barriers at patients home) and causing an increased length of stay, also due to the difficulties to transfer the patients to nursing home, and to the difficulties experienced by the patients to obtain all the necessary equipment. However, none of the respondents reported an impact on patients outcomes, especially in daily living independence.
Conclusions:: The outpatients activities have been impacted too and this reflected in an increase of complications related to SCI, in particular pressure ulcers, pain, spasticity, anxiety and depression.
A CASE OF NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOSD) AND ACUTE MYOSITIS FOLLOWING SARS-COV-2 INFECTION

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Background and Aims:: Neurological manifestations of COVID-19 have been described. We report a case of seropositive NMOSD and acute myositis following SARS-CoV-2 infection.

Methods:: A previous healthy 35-years old man was admitted for NORB, a month after paucisymptomatic SARS-CoV-2 infection. Nasopharyngeal tests for SARS-CoV-2 was negative and serological IgG and IgM were positive. The neurological examination showed left eye blindness and myalgia. Blood examination showed elevated CK (>1000 UI/l), positive ANA (1:640) and anti-TPO (>1300 U/ml). Brain MRI showed T2/FLAIR left optic nerve hyperintensity with contrast enhancement. The EMG revealed signs of acute myogenic damage. He received intravenous methylprednisolone with poor recovery on vision but full recovery on muscle symptoms. Four months later he present NORB in contralateral eye; MRI showed optic chiasm hyperintensity, serum anti-AQP-4-antibodies were positive, EMG and CK were normalized. The patient received intravenous steroids and Immunoglobulins and started rituximab. Nevertheless, three months later he developed the area postrema syndrome, he was retreated with intravenous steroids and immunoglobulins and achieved a complete recovery. In March 2021, he underwent the second course of rituximab with clinical and radiological stability.

Results:: The patient was diagnosed with seropositive NMOSD, presented with recurrent NORB and area postrema syndrome, associated to acute myositis and autoimmune tiroiditis after SARS-CoV-2 infection.

Conclusions:: We supposed that SARS-CoV-2 may cause a post-infectious autoimmune response directed against AQP4 and other target (the muscle, the tiroid gland). Post-infectious autoimmunity is a potential mechanism in a subset of patients with COVID-19-related neurologic disease. Further research is needed to clarify this association.
THE IMPACT OF THE COVID-19 PANDEMIC ON CHILDREN AND FAMILIES UNDERGOING EPILEPSY SURGERY

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Background and Aims:: The COVID-19 pandemic has had a significant impact on how healthcare is delivered to patients with epilepsy. Epilepsy surgery is a strategy with high reported satisfaction rates but can be a stressful road for patients. We aimed to determine significant challenges faced by the families of children undergoing epilepsy surgery during the pandemic.

Methods:: Cross-sectional study that included pediatric patients that underwent epilepsy surgery at Children’s Hospital/LHSC comparing two groups. We collected data at follow-up using a prespecified questionnaire asking to evaluate difficulties on a scale of 0-4. Questions focused on seizure activity, concerns over procedure delay, changes in hospital regulations, fear of exposure to COVID-19 and virtual appointments.

Results:: Thirty-five surgeries were planned from March 2020 to February 2021, but only 12(34%) were performed (60% decrease vs. 2019). Out of the 12 families, 11 answered the survey. The most challenging aspect was ongoing seizure activity while waiting for surgery expressed by 10/11 families. Four caregivers ranked it as considerably/extremely challenging. Limitations in the number of allowed-in-hospital visitors were deemed significantly/extremely challenging by 5/11(45%), and fear of being exposed to COVID-19 was low in 6/11(54%) families. Two families reported extreme challenges while telemedicine consults.

Conclusions:: These findings show how the pandemic impacted epilepsy surgery patients. The number of surgeries was reduced considerably throughout the pandemic, with subsequential increased seizure activity and emotional burden on patients. Parents with no additional support expressed the most challenges but felt safe with the implemented COVID-19 measures. Most families were comfortable using telemedicine protocols. Limitations include a small sample size.
Background and Aims:: In March 2020, WHO declared Novel Coronavirus Disease (COVID-19) outbreak to be a pandemic. All countries were given the call to take prompt actions to reduce spread of infection and save lives. The prevalence of the disease rose exponentially world wide. When it comes to the new SARS COVID 19, the understanding of the disease was poor, especially among the non medical folk. Social media was flooded with information and several of them were not tested for authenticity. Accurate information is the key to protect oneself, one's family as well as one's society and break the chain in the spread of the misinformation and the disease.

Methods:: In June 2020, we conducted a study among the students of an engineering college to assess the knowledge about Covid 19. An online questionaire with 29 open ended questions was mailed to 700 students and faculty. The questionaire included demographics, fund of information, risk factors, prophylaxis, protection and mode of transmission of SARS-CoV-2.

Results:: 416 subjects ages ranging from 18- 53 years participated in the study. 22.8% believed that COVID-19 is caused by bacteria. 12.5% believed that it affects the elderly only. 41.1% believed it is airborne. 37.7% considered it unsafe to go to hospitals for medical attention though 80.5% believed that if they have cough or fever, they should get tested. 46.6% believed a vaccine for COVID-19 has already been launched.

Conclusions:: Our study results showed several lacunae in the levels of knowledge regarding COVID-19 except for the co-morbidities being risk factors for COVID-19.
MYOSITIS ASSOCIATED TO COVID-19 MIMICS AN ACUTE EXACERBATION IN MYASTHENIA GRAVIS PATIENT

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Background and Aims:: Coronavirus disease 2019 (COVID-19) is an acute infection of the respiratory tract spread into a global pandemic. Emerging case reports have described neurological manifestations in patients with COVID-19 infection including headache, seizure, Guillian-Barré syndrome and encephalitis. Here we report a case of a patient affected by myasthenia gravis (MG) who developed a severe myositis post COVID-19.

Methods:: A 45 years-old woman affected by MG since she was 30, presented to our Neurological Department reporting severe weakness prevalent in upper limbs, diffuse myalgia, dysphagia and dyspnea started two months after COVID-19 infection.

Results:: We administered intravenous immunoglobulin (IVIG) in suspecting of MG aggravation, however without clinical improvement. A full blood panel showed elevated Creatine-Phosphokinase (CPK) and Lactate-dehydrogenase (LDH) levels. Autoimmune screening revealed low level of complement C3, positive antibodies anti-Nuclear (ANA) and anti-Phospholipide (aPL), included anti-Cardiolipin (aCL) and anti-β2-glycoprotein I (aβ2GPI). Electromyographic (EMG) examination showed: diffuse spontaneous activity with positive sharp wave (PSW), fibrillation potential, small and short motor unit action potentials (MUAPs) in quantitative analysis, suggesting acute myopathic pattern. We performed therapy with intravenous Methylprednisolone for five days with full clinical recovery. One month later, EMG features were significantly improved.

Conclusions:: Viral infection is a well-known cause of myositis described also in patients with COVID-19, probably due to the expression of ACE-2 on the muscle cells. To our knowledge, this is the first case in literature of myositis associated to COVID-19 infection in MG patients. We want to underline how myositis symptoms could mimic an acute exacerbation of MG leading to harmful misdiagnosis.
IMPACT OF COVID-19 PANDEMIC ON ACUTE STROKE CARE-DATA ANALYSIS FROM THE RES-Q REGISTRY 2020 IN N. MACEDONIA

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Background and Aims:: Since 2017, the Department of Urgent Neurology at the University Clinic of Neurology in N. Macedonia has implemented the Angels Initiative and the RES-Q Registry, in order to evaluate and optimize the quality of care of acute stroke patients. The aim was to analyze acute stroke data in 2020 and evaluate the impact of COVID-19 pandemic on acute stroke care.

Methods:: Database categories entered in 2020 in the RES-Q registry were compared in 4 consecutive quarterly periods. We used a statistical analysis to estimate the NIHSS reporting, CT-time and the number of IVT procedures; carotid artery imaging, prescription of antithrombotics and statins, median discharge mRS and median hospital stay.

Results:: Quarterly analysis showed significantly reduced number of acute stroke admissions by 34% and 85%, decreased number of IVT procedures by 40% and 100% in the 3rd and 4th quarter, respectively (p<0.05). DTN time was prolonged by 30.5% in the 3rd quarter (p<0.05). Carotid artery imaging was reduced by 100% in the 4th quarter (p<0.05). Median hospital stay was prolonged for 8 days in the 4th quarter (p<0.05). These findings were consistent with the increased number of COVID-19 patients and implemented epidemiologic measured in the country in the second half of 2020. Other analysed parameters of quality of stroke care were not affected (p>0.05).

Conclusions:: COVID-19 pandemic has had significant impact on acute stroke care with reduced number of admissions and decreased number of IVT treatment with prolonged DNT and longer hospital stay.
BENIGN COVID-19 IN AN AGGRESSIVE CASE OF AQUAPORIN-4 NEUROMYELITIS OPTICA TREATED WITH TOCILIZUMAB.

**Background and Aims::** Neuromyelitis optica (NMO) with antibodies (Abs) against aquaporin-4 (AQP4) is an astrocytopathy with severe spinal attacks resulting in mobility impairment. Relapse prevention is mandatory with immunosuppressants or anti-CD20 monoclonal Abs. Aggressive AQP4-Ab NMO could benefit by blocking the interleukin 6 (IL6) pathways with Tocilizumab. This IL6 inhibitor improved patient outcome in severe COVID-19 pneumonia.

**Methods::** Our case is a 52-year-old woman severely disabled by aggressive AQP4 NMO unresponsive to rituximab. One year after disease onset, she was bed-bound with tetraparesis related to several spinal attacks, mostly at the cervical level. She was repeatedly treated over the months with intravenous steroids, plasma exchange, and immunoglobulins. Meantime, two cycles of cyclophosphamide, and then three administrations of rituximab obtained no conclusive benefit on the inflammatory activity. Consequently, she started a third-line treatment with tocilizumab and finally stabilized after the two administrations.

**Results::** On intensive rehabilitation, she progressively improved her right arm function and became able to be on wheel-chair. In this context, she developed fever and cough with no evidence of pneumonia and recovered in one week. Two nasopharyngeal swabs for SARS-CoV-2 resulted positive (day 1 and day 10) and a third negatized at day 14. This mild COVID-19 infection resolved spontaneously without sequelae. On day 15 she continued with her monthly Tocilizumab infusions.

**Conclusions::** In our case, Tocilizumab was effective in preventing NMO relapses as a third-line treatment and resulted safe during COVID-19 pandemic.
COVID-19 ASSOCIATED STROKE: CLINICAL FORMS AND FEATURES OF THE DISEASE

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Background and Aims: To study the forms and features of the clinical duration of ischemic stroke in patients with coronavirus infection (COVID-19).

Methods: Analyzed 76 cases of ischemic stroke in two groups. The main group (n=34; 44.7%) patients with ischemic stroke, in combination with COVID-19. The comparison group patients (n=42; 55.3%) with ischemic stroke without clinical and laboratory confirmations of COVID-19. For confirmation of the diagnosis were used MSCT of the brain and laboratory PCR diagnostics.

Results: The average age of patients in the main group was 65.4±2.3 and in the control group was 68.7±1.8 years old. Comparison by sex showed that in both groups was a significant predominance of men in proportion with 2:1. The subtypes of ischemic stroke in the main group was dominated with unspecified and cardioembolic subtypes – 47.1% (n=16) and 23.5% (n=8), respectively. Atherothrombotic and lacunar subtypes were in 20.6% (n=7) and 8.8% (n=3) patients, respectively. In control group patients, the proportion of atherothrombotic subtype was 54.8% (n=23), cardioembolic – 19.0% (n=8), unspecified – 9.5% (n=4) and lacunar – 16.7% (n=7). The severity of ischemic stroke according to the NIHSS scale in the main group averaged 20.13±8.16 more than in the control group 12.3±7.61, P <0.001. Assessment of the disability degree according to the Rankin scale showed that in the main group higher number than the control group with 6.00 and 4.00 respectively.

Conclusions: In ischemic stroke with COVID-19 patients, age characteristics have not been established. The predominant subtypes of the ischemic stroke in COVID-19 patients were unspecified and cardioembolic subtypes.
DE NOVO STATUS EPILEPTICUS IN COVID-19

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Background and Aims:: Neurological complications have been described in COVID-19. We present three COVID-19 patients (2 men, 74-78 years; woman 63 years) with acute de novo status epilepticus (SE) presentation in the period between November 2020 and March 2021.

Methods:: All patients (nasopharyngeal swab for SARS-CoV-2 was positive, chest CT showed interstitial pneumonia) presented sudden onset of seizures/confusional state. Only one patient had a past medical history of epilepsy with seizure freedom from 35aa. Two patients had negative CT brain; scalp EEG showed widespread epileptic activity; in one patient the EEG showed right temporal PLEDS and positive brain CT / MRI for right temporal-basal inflammatory lesion. CSF analysis for SARS-Cov-2 and neurotropic pathogens was negative.

Results:: All patients were treated according to COVID-19 protocols (clexane, corticosteroids), O2 (as needed), Aciclovir (10mg/Kg/day); intravenous immunoglobulin (0.4g/Kg/day) were administered in one patient; benzodiazepines and antiepileptic drugs (Levetiracetam, Valproic Acid, Lacosamide according to SE protocols) were used as rescue-therapy. All patients presented seizures remission; one patient experienced rapid overall clinical improvement, while the other, despite the neurological improvement, showed a worsening of the pulmonary-respiratory condition.

Conclusions:: The SE/confusional state can be the initial presentation of SARS-CoV-2 infection. A mechanism related to the systemic inflammatory syndrome in COVID-19 has been hypothesized, but further data are needed for understanding the SE COVID-19 related pathogenetic mechanisms. Early EEG is decisive for the correct diagnostic-therapeutic process, especially in non-convulsive forms.
Background and Aims: In COVID-19, blood clotting increases, the process of thrombus formation is the cause of aseptic thrombosis of the cavernous sinus. A decreased immunity and inflammatory processes of the face, paranasal sinuses also leads to septic complications. Aim. Diagnostics of thrombosis of cerebral vessels and venous sinuses in patients after COVID-19

Methods: In the multidisciplinary clinic of the TMA in 36 patients with a diagnosis of cavernous sinus thrombosis. The average age of patients was 60 ± 8 years, of which 26 were women (57.8%) and 19 were men (42.2%). All patients underwent MRI of the brain with angiography (MRT GE Optima 1.5 Tesla, USA)

Results: 38% developed non-infectious thrombosis, 52% of patients developed an inflammatory complication of the maxillofacial region after the acute phase of COVID-19 led to cavernous sinus thrombosis. With MRI in standard modes, signs of venous thrombosis can be detected: an increase in the signal intensity from the altered sinus (the most cavernous sinus, rarely the inferior cavernous and sigmoid sinuses), the venous sinuses are asymmetric. In 84%, blood flow in the remaining sinuses is preserved. When conducting MR venosinusography, a decrease in the signal from the blood flow along the affected side, as well as a compensatory increase in the signal from the blood flow, and vasodilation on the opposite side are revealed.
Conclusions: MRI contrast angiography is an informative method for determining the state of blood supply and the place of a thrombus in a vessel. In the treatment complications, it is necessary to restore the blocked vascular permeability.
CASE REPORT: COVID-19 AND BENIGN INTRACRANIAL HYPERTENSION

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Background and Aims:: Neurological complications are not rare in patients who survived COVID-19. On the other hand, ophthalmologists say that ocular manifestations should not be neglected.

Methods:: We report the case of a 45-year-old male patient COVID-19 positive one month ago, without any other comorbidities, who presents in the Emergency Room in a stuporous state and bilateral midriasis after a tonic bilateral epileptic seizure. Two hours later he was lucid and oriented, without any focal neurological deficit but bilateral midriasis persisted. The patient complained severe, holocranial throbbing headache with dizziness, nausea and significant visual blurring. Ophthalmological examination reveals bilateral optic disc oedema, peripapillary hemorrhagic petechiae and venous tortuosity. Brain MRI, Angio- MRI and EEG resulted normal. The patient is treated with a high-dose of corticosteroids for three days and acetazolamide. After treatment he has no other complaints and the headache is less severe. We scheduled a follow-up with fundoscopy, after being treated with acetazolamide for 10 days.

Results:: Headache is one of the frequent neurological symptoms associated with COVID-19. In the absence of evidence of infectious or vascular disease, pseudotumor cerebri should be considered. Several studies suggest that patients with COVID-19 have vascular retinal lesions, including flame shaped haemorrhages, peripapillary petechie and acute retinal ischaemia.

Conclusions:: Further research is needed for COVID-19 and the possible neurological or ocular complications. It is important to consider pseudotumor cerebri in a patient with severe headache after COVID-19 and to perform a fundoscopy if indicated.
COHORT STUDY OF NEUROLOGICAL COMORBIDITIES AND COVID-19-RELATED CASE FATALITY

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Background and Aims:: Neurological involvement in Coronavirus disease-2019 (COVID-19) is widely recognized. However, the role of pre-existing neurological comorbidities in modulating COVID-19-related mortality still remains unclear. This cohort study evaluates the COVID-19-related case fatality rate (CFR) of patients with neurological diseases.

Methods:: We retrospectively evaluated all patients consecutively admitted to our hospital with a diagnosis of COVID-19 between March and April 2020. Demographic and clinical data, including 30-day survival, were retrieved. We used a multivariate regression analysis to estimate the association between neurological diseases and COVID-19-related mortality. Then, we compared the CFR and survival curves of two cohorts (patients suffering vs. those not suffering from neurological disease), matched through the propensity score (PS). Age and other comorbidities were considered for PS calculation. We applied a 1:1 matching for the entire neurological cohort and, separately, for cerebrovascular, neurodegenerative, and other neurological diseases.

Results:: Among 332 patients, 75 (22.6%) were affected by neurological disease (n=29 cerebrovascular, n=26 neurodegenerative, n=20 others). From the regression analysis, they resulted with a 2.5-fold increase of COVID-19-related mortality. From the cohort analysis, CFR resulted 2-fold higher in patients with neurological disease (48.0% vs. 24.0%; p=0.002). CFR was significantly higher in patients with neurodegenerative diseases compared to matched individuals (73.9% vs. 39.1%; p=0.017), while CFR increase in patients with cerebrovascular diseases did not reach full statistical significance (48.3% vs. 41.4%; p=0.597).
Conclusions: Neurological comorbidities, in particular neurodegenerative diseases, increase significantly COVID-19-related case fatality, indicating a clear priority for viral screening, access to care facilities and vaccination in these populations.
NEUROLOGICAL MANIFESTATIONS IN PATIENTS WITH SYMPTOMATIC COVID-19 ADMITTED TO THE BAFOUSSAM REGIONAL HOSPITAL, CAMEROON

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Background and Aims:: Although the main manifestations of COVID-19 are respiratory, several neurological symptoms and complications have also been reported. The pandemic seems to have some epidemiological specificities in sub-Saharan Africa, and this may be reflected in the type and frequency of neurological symptoms. This study aimed to report neurological manifestations associated with symptomatic COVID-19 in a sub-Saharan African setting.

Methods:: We conducted a retrospective review of symptomatic PCR-confirmed COVID-19 cases admitted to the Bafoussam Regional Hospital between March and September 2020. Patients’ files were reviewed at discharge by a consultant neurologist. Socio-demographic characteristics, co-morbidities, symptoms on admission, neurological symptoms during hospitalization, management, and in-hospital outcome were recorded. Comparisons between patients with and without neurological symptoms were performed using Fisher’s exact and Mann-Whitney U test.

Results:: We enrolled 177 symptomatic patients (68% men). Mean age was 54.6 ± 17.8 years (range 2-99 years). Co-morbidities were present in 57.6% of patients, including hypertension (27.1%) and diabetes mellitus (25.4%). Neurological symptoms were found in 113 (63.8%) patients. The most frequent were headache (39.0%), myalgia (35.6%), anosmia (11.9%), impaired consciousness (10.7%) and delirium (5.6%). Regarding the presenting symptoms, fever was more frequent in patients with neurological symptoms than in those without (81.4% versus 50.0%, p< 0.001), while digestive symptoms were less frequent in patients with neurological symptoms (0.9% versus 9.4%, p= 0.004).

Conclusions:: Neurological manifestations are frequent and heterogenous in patients with symptomatic COVID-19. Further studies are needed to clarify the pathophysiology of neurological symptoms in COVID-19 and their impact on patients’ long-term outcome.
THE CLAISTRUM SIGN IN A PARAINFECTIOUS COVID 19 ENCEPHALITIS

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Background and Aims:: Various neurological symptoms and manifestations associated with COVID-19 have been described. Imaging findings on brain MRI scans were reported as being unspecific, apart from acute necrotizing encephalopathy. Here, we present the first Italian case of parainfectious autoimmune encephalitis in a Covid 19 patient with a specific MRI pattern, responsive to steroid treatment.

Methods:: An otherwise healthy 61-year-old woman presented to the Emergency Department for an acute confusional state with drowsiness and impaired speech.

Results:: Even in the absence of fever or respiratory symptoms a RT-PCR test for SARS-CoV-2 using a nasopharyngeal swab was positive. Chest CT disclosed a mild interstitial pneumonia. Arterial blood gases was normal. Neurological examination exhibited mutism, slowness in executing orders, bilateral postural tremor, upper right arm weakness. Electroencephalography showed generalized delta slowing. Cerebrospinal fluid analysis revealed normal white-cell count, a mild increased protein concentration with negative test results for neurotropic viruses and also for Sars-CoV2. Tests in serum and CSF were negative for antineuronal antibodies whereas the serological test for Covid 19 was positive. Brain MRI showed FLAIR hyperintensities bilaterally but especially on the left side of the putamen, the claustrum, the insula cortex and the fronto-temporal cortex, without diffusion reduction or postcontrast enhancement. Thus, suspecting an autoimmune encephalitis, an high-dose steroid treatment was started followed by a tapering per os and a complete clinical and neuroradiological recovery was observed.

Conclusions:: The peculiar imaging pattern with the claustrum sign identified in our Covid 19 patient probably reflects an autoimmune phenomenon that might resolve with prompt recognition and appropriate therapy.
INSOMNIA IN POST COVID-19 HOSPITALIZED PATIENTS

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Background and Aims:: to describe the presence of sleep disorders in patients after hospitalization for COVID-19. 117 studied people under follow-up at the National Institute of Respiratory Diseases (INER) in the outpatient clinic. Patients with mild, moderate or severe symptoms of Covid-19 was carried out. A multiple regression model with backward selection was carried out to evaluate the effects of each of the neurological symptoms as risk factors in the development of insomnia. P values less than 0.05 were considered statistically significant.

Methods:: To descriptive the analysis of Mexican population patients with mild, moderate and severe symptoms of Covid-19 was carried out. A multiple regression model with backward selection was carried out to evaluate the effects of each of the neurological symptoms as risk factors in the development of insomnia. P values less than 0.05 were considered statistically significant.

Results:: 117 subjects were included, 36 (31%) women and 81 (69%) men, 58 ± 13 years of age, divided between groups according to severity, mild n = 17 (15%), moderate n = 27 (23%) and Severe N = 73 (62%) The comorbidities between the included groups did not present statistical differences, DM 2, overweight, Obesity, morbid obesity, heart disease, pneumopathy and hypothyroidism. Post-covid insomnia, pre-covid heart disease regardless of the groups with a prevalence of 9.9% with a p = 0.041. Patients with cognitive complaints had a 68.4% prevalence of insomnia p = 0.015. In patients with anxiety, the prevalence of insomnia was 68% p = 0.001.

Conclusions:: The symptoms found during covid-19 in our population are similar to those published in the international literature. The patients with the highest prevalence of insomnia were have pre-covid heart disease, anxiety, and cognitive complaints.
ANALYSIS OF DELAYED ADMISSION TO HOSPITAL IN ACUTE STROKE PATIENTS BEFORE AND DURING THE PANDEMIC COVID-19 IN BISHKEK, KYRGYZSTAN

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Background and Aims:: Stroke services worldwide experienced the drop and barriers in admissions of patients to acute stroke departments in COVID-19 pandemic time. We aimed to analyze how lockdown due to the pandemic affected the number of admissions of acute stroke.

Methods:: Logistical parameters in 479 medical records of patients with acute stroke, examined by emergency teams of the Emergency Medical Center in Bishkek (EMCB) were analyzed retrospectively in 4 months: December 2019, January 2020 ( prepandemic months) and July and August 2020 (highest COVID-infection rates) in Bishkek, Kyrgyzstan.

Results:: Only 50,1% of cases were recognised as “strokes” by the emergency dispatcher and the correct team was sent to the patient. The mean time from the stroke onset till emergency team arrival was 15.6 ± 15.4 hours and the shortest median time (4.5 h) was in a group with the highest NIHSS score, p=0.01. In July 2020 (highest COVID infection rates in Kyrgyzstan) in 27.8% of cases an accepted stroke call was transferred by the dispatcher to the ambulance team within 90 minutes. 27.7% of stroke patients refused to be hospitalized in the pandemic time and in 8.3% of cases, patients were not hospitalized due to the lack of places in duty hospitals.

Conclusions:: Prolongation in aid to stroke patients is caused with low stroke recognition by population,
overload of emergency teams and patients refusal of the hospitalisation. COVID-19 pandemic in Kyrgyzstan though stimulated to train 91 emergency doctors in NIHSS and this scale was implemented in pandemic in prehospital settings.
AUTOIMMUNE LIMBIC ENCEPHALITIS RELATED TO SARS-COV-2 INFECTION: CASE-REPORT AND REVIEW OF THE LITERATURE

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Background and Aims:: SARS-CoV-2 infection is associated with a wide spectrum of neurological complications, including encephalitis. Most cases showed features consistent with a central nervous system (CNS) cytokine-mediated damage. However, few cases arguing for an autoimmune mechanism have been described, mainly as single reports or sparse in large case series involving other CNS manifestations. In this paper, we described a case of definite autoimmune limbic encephalitis (LE) COVID-19 related and reviewed the existing literature on other reported cases.

Methods:: Two weeks after the onset of COVID-19 infection, a 74-year-old woman presented with subacute confusion and focal motor seizures with impaired awareness, starting from left temporal region. Cerebrospinal fluid analysis revealed hyperproteinorrachia. Brain MRI showed bilateral T2/FLAIR hyperintensities in both hippocampi and total body PET/TC scan revealed hypermetabolism in basal ganglia bilaterally. A diagnosis of autoimmune LE was made. Thus, high dose corticosteroids and antiseizure medications were started, with a marked improvement of neurological conditions.

Results:: We systematically reviewed the literature to identify all well-documented cases of definite autoimmune LE (according to Graus criteria) in patients with COVID-19 infection, identifying other five cases exhibiting a good response to immunomodulating therapy.

Conclusions:: A very limited number of autoimmune LE have been described until now. It is important to monitor neurological symptoms in COVID-19 patients and to consider the possibility of an autoimmune LE, in particular when altered mental status and seizures appear late in the disease course. This allows to promptly start the appropriate treatments and avoid unnecessary delays.
Background and Aims:: Background: SARS-CoV-2 infection has been associated with various neurological manifestations. Since patients affected by SARS-CoV-2 infection present coagulation and immune system dysregulation, ischemic or haemorragic stroke is not uncommon, irrespective of respiratory distress. The occurrence of focal neurological deficits during SARS-CoV-2 infection suggests acute stroke but if other symptoms like headache, cortical blindness, seizure and altered mental status are present, Posterior Reversible Encephalopathy Syndrome (PRES) should be also considered in the differential diagnosis. Antithrombotic treatment, the alteration of endothelial function and coagulopathy due to COVID-19 and PRES leading to the breakdown of blood-brain barrier may then contribute to the occurrence of brain haemorrhage.

Methods:: We describe the case of a COVID-19 patient who developed bilateral haemorrhagic stroke of occipital lobes suggestive of haemorrhagic PRES. We then reviewed the available literature about haemorrhagic evolution of PRES in COVID-19.

Results:: We describe clinical and radiological features of five COVID-19 patients who developed haemorrhagic PRES.

Conclusions:: Coagulopathy and endothelial dysfunction resulting from the massive release of cytokines during the host immune response may be key factors in the pathogenesis of COVID-19-related PRES. Antithrombotic therapy and the leakage of the BBB can subsequently increase the risk of haemorrhagic transformation of the lesioned brain tissue. A prompt diagnosis of PRES is mandatory, since the timely interruption/reversal of antithrombotic therapy may be a key determinant for a good prognosis.
COVID-19 AND STROKE: CASE REPORT

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Background and Aims:: Introduction: Covid-19 is associated with common neurological diseases including stroke. It is believed that covid-19 can cause hypercoagulability state which can induce thrombotic events which may predispose for stroke. Objective: To document the effect and outcome of Covid-19 infection in patients with stroke.

Methods:: A 62 years Sudanese male known diabetic, hypertensive, hypercholesteremia, presented to the casualty with left sided weakness. Full medical history and physical examination was done, routine and specific investigations were done

Results:: The patient presented with left sided weakness, started suddenly. Both left upper and lower limbs were affected at the same time. He became completely paralyzed within less than six hours. Deviation of the mouth to the right side is noted. Physical examination reviled weakness in the left side of the body (left upper and lower limbs) where the power was grade zero in both limbs plus hypotonia and areflexia. His wife mentioned that two days prior to admission he started to complain of loss of taste, sore throat and intermittent high grade fever and for that he was given antimalarial without response. investigations were: Complete hemogram rather than lymphopenia no abnormalities were detected, ECG: left ventricular hypertrophy plus left access deviation, Chest X-ray showed evidence of cardiac enlargement and mid zonal pneumonia, chest showed an evidence of bilateral ground glass appearance. Test for COVID-19 was positive, CT brain showed an evidence of right Cerebral infarction, D-dimer is elevated.

Conclusions:: Strokes are being reported as a complication of COVID-19 due to the hypercoagulability state induced by Covid-19 infection.
ATYPICAL CEREBROVASCULAR COMPLICATIONS OF COVID-19

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Background and Aims:: Many neurologic complications were recognized with COVID-19. Cerebrovascular disorders were one of these complications. In our case report we describe two cases presented with atypical cerebrovascular presentations associated with COVID-19. The first case presented with right cavernous sinus thrombosis, right cavernous portion of the internal carotid artery partial thrombosis with bilateral basal ganglia microbleeds. The second case presented with multiple hemorrhagic infarctions as a first presentation.

Methods:: Case 1: 45 years old male admitted to the emergency unit complaining from fever, associated with respiratory symptoms, and generalized body aches. CT chest showed bilateral ground glass appearance (CORAD-5). SARS-CoV-2 PCR sample from nasopharyngeal swab was positive. Two weeks later patient developed painful diminution of vision in the right eye, which progressed to complete loss of vision. Later, patient developed right ophthalmoplegia, right 5th and 7th nerve palsies, left sided hemiparesis, bulbar symptoms with marked emotional liability. MRI, MRA and MRV showed right cavernous sinus thrombosis, right partial thrombosis of carotid artery and bilateral basal ganglia microbleeds. Case 2: COVID-19 positive 62 old female presented to ER unit with Fever and acute onset confusional state. MRI Brain showed multiple hemorrhagic infarctions (figure 1).
Results: The symptoms of the first case like bulbar, left sided heaviness were improved, while loss of vision and ophthalmoplegia did not improve. The second patient died few hours after diagnosis.

Conclusions: Cavernous sinus thrombosis and hemorrhagic infarctions could be associated with or complicate COVID-19 infection.
THE CORRELATION BETWEEN DEPRESSION AND ANXIETY WITH COGNITIVE FUNCTION OF NURSE IN ISOLATION ROOM FOR CORONAVIRUS DISEASE-19 IN RSUP HJ. ADAM MALIK MEDAN

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Background and Aims:: Coronavirus disease-19 has psychological impact on health workers, depression and anxiety are the most common psychological problems and may affect cognitive function. The research aimed to determine the correlation between depression and anxiety with cognitive function in nurses working in the isolated ward and to compare them with nurses not working in isolated ward.

Methods:: This study was a cross-sectional study using consecutive total sampling technique, at Covid-19 isolated ward at General Hospital H Adam Malik Medan, March 2021. We included all nurses providing services to Covid-19 patients. We assessed depression, anxiety, and cognitive function using BDI, BAI, and MocA-Ina.

Results:: This study involved 72 participants. The mean age of nurses working in the isolated ward was 33 (24 - 52) years old. The Median of BDI 5 (0 - 37), BAI 3 (0 - 22), and MocA-Ina 26 (18 – 30). There was correlation between depression and cognitive function (p = 0.02, r = -0.273), no correlation between anxiety and cognitive function (p = 0.46, r = -0.088). There was no difference in depression (p = 0.324), anxiety (p = 0.332), and cognitive function (p = 0.210) between nurses working in the isolated ward and nurses not working in isolated ward.

Conclusions:: Depression is significantly associated with cognitive functions in nurses working in the isolated ward. These results suggest that depression intervention is needed to prevent cognitive dysfunction.
TRIGEMINAL NEURALGIA POST COVID 19. PRELIMINARY REPORT AND CLINICAL CONSIDERATION

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Background and Aims:: Covid-19 is a single RNA virus that enters the host cells after binding to the Angiotensin-converting enzyme 2 (ACE2). The symptomatic picture of SARS-CoV2 is dominated by respiratory disease. However, the spread of the virus, is not circumscribed considering that ACE2 receptor expression is also detected in other tissues, including the CNS. Neurological impairment is more likely in patients with more severe infection, and the most frequently encountered neurological pathologies were acute cerebrovascular disease, impaired consciousness, and impaired taste and sense of smell. Painful neuralgia was less frequent. The aim of our study is to evaluate the possible correlation between Covid-19 infection and trigeminal neuralgia.

Methods:: From November 2020 to March 2021, 10 cases of trigeminal neuralgia arising after Covid-19 infection were observed. 7 women and 3 men aged 30-55 years with mild-to-moderate infection that did not require hospitalization. Painful symptoms mainly involved the II branch of the V cranial nerve. All patients had brain magnetic resonance imaging (MRI), blink reflex, and VAS pain scale, performed

Results:: Neuroradiological and neurophysiological investigations showed no pathological data, while pain assessment with VAS showed values between 6 and 8. All patients underwent medical therapy with CBZ.

Conclusions:: The loss or reduction of taste and/or smell could suggest that the virus reaches the CNS through the olfactory nerve, localizing in the brainstem. This could also explain the involvement of other cranial nerves
Background and Aims:: Introduction: Guillain-Barré syndrome is an acute polyradiculoneuropathy which is immune mediated. It’s considered as a life-threatening by the respiratory affection and the dysautonomia. It is commonly reported as an adverse event after campylobacter jejuni infection and following vaccination.

Methods:: We report two cases of GBS, after receiving the first dose of Astrazeneca COVID-19 vaccine.

Results:: Cases description: First case of a 70 years old woman, presenting progressive, symmetric, ascending flaccid tetraparesis with bladder dysfunction which have occurred three weeks after the first dose of Astrazeneca covid-19 vaccine. The cerebrospinal fluid showed an albuminocytologic dissociation, electrophysiological studies showed an acute inflammatory demyelinating polyradiculoneuropathy. Second case of a 68 years old woman, presenting three weeks after the first dose of Astrazeneca covid-19 vaccine a progressively descending, symmetrical and synchronous tetraplegia, preceding 4 days before by diffuse headaches with multiple cranial pairs affection and bladder dysfunction. The cerebrospinal fluid showed an albuminocytologic dissociation, electrophysiological studies showed an acute inflammatory axonal and demyelinating polyradiculoneuropathy.

Conclusions:: Conclusion: Many cases of GBS after vaccines has been reported including one case following Pfizer covid-19 vaccine, yet the physiopathological mechanisms are not completely elucidated.
EFFICACY OF AMANTADINE IN PATIENTS HOSPITALIZED WITH COVID-19: STUDY PROTOCOL OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Background and Aims:: In 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began circulating worldwide and caused the coronavirus disease 2019 (COVID-19). To date, no highly effective treatments are available. Amantadine, an old, cheap and safe drug, is currently used for Parkinson’s disease and multiple sclerosis, as well as being known for its antiviral action. Recent reports suggested a possible efficacy of amantadine against SARS-CoV-2. The proposed treatment, upon demonstration of efficacy and safety, could be easily administered even in developing countries for its low cost (Eudract n. 2021-001958-60).

Methods:: Enrollment of 380 participants requiring hospitalization with a recent onset of mild or moderate COVID-19. Two arms with 190 patients each will be treated with standard of care (SOC) + amantadine or SOC + placebo for 14 days. Patients will be monitored until discharge and assessed at day 30, 60 and 90 after randomization. Upon progression, patients will be followed up, but treatment will be discontinued. Study endpoints: 30 day mortality (primary), 30 day admission to Intensive Care Unit or death, worsening of clinical symptoms within 14 days, negativization for SARS-CoV-2 at day 14.

Results:: A reduction of 30-day mortality from 15% (SOC + placebo) to 7% (SOC + amantadine) is hypothesized.

Conclusions:: There are few independent and valid studies successfully concluded during the pandemic. The hope is that the evidence from this study will contribute to increasing the treatment options for COVID in the early stages of infection.
THE ITALIAN NATIONAL SURVEY ON COVID-19 IN NURSING HOMES DURING THE FIRST WAVE OF THE PANDEMIC

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Background and Aims:: The SARS-CoV-2 pandemic had a strong impact on the most vulnerable categories such as older people, who paid the highest price. Nursing homes (NH) have been the epicenter of the pandemic. In NHs about a quarter of residents have dementia.

Methods:: The survey started on March 24, 2020 and reached 3292 out of the 3417 NHs present in Italy (source: the Dementia Observatory of the Italian National Institute of Health).

Results:: As of May 5, 2020, 1356 NHs (41.2% of the total) filled in the questionnaire via web, on a voluntary basis. A total of 29% of NHs reported SARS-CoV2 infection among residents (mean: 18.7 cases per 100 residents, range: 0.5-86.9) or staff, with frequency reaching 68% when including people with flu-like symptoms. Overall, 7.4% of the 9154 deceased subjects and 18.2% of the 5292 hospitalized had COVID-19 (33.8% and 38.2% respectively had flu-like symptoms). Fatality rates by region were higher than those observed in the general population. The main reported critical issues were lack of personal protective equipment (77.2%), inability to perform swabs (52.1%), absences of health personnel (33.8%), and difficulties in isolating (26.2%) and transferring residents (12.5%). All these factors resulted significantly associated with the spreading of COVID-19 in the NHs.

Conclusions:: The low response rate limits the generalizability of results, that were probably underestimated in terms of mortality and hospitalization rates, according to ad hoc analysis. This survey was the first major attempt to highlight critical issues and needs in NHs.
COVID-19 AND DEMENTIA: RECOMMENDATIONS FROM THE ITALIAN DEMENTIA NATIONAL PLAN WORKING GROUP

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Background and Aims:: Worldwide, about a fifth of those who died with COVID-19 were affected by dementia. A high number of excess deaths among people with dementia living in Italy was documented during the first wave of the epidemic. Based on such data, the Italian Dementia National Plan Working Group produced a report addressed to caregivers and healthcare professionals for the management and support of patients with dementia during the pandemic.

Methods:: Between September and October 2020, 11 online meetings were organized by the members of the Working Group. Documents produced by national and international Organizations were collected and analyzed together with the specific scientific literature on dementia and COVID-19. After reaching a consensus, recommendations for different health care settings were provided.

Results:: The report is structured into four sections: 1) reorganization of clinical and social care activities (e.g. swab execution procedures, management of behavioral disorders, accessibility to invasive treatments); 2) assistance in home settings; 3) care and support in day centers and residential structures (e.g. management of group activities in full safety, visits by family members); 4) training for health and social personnel (e.g. training on frequent atypical presentation of COVID-19 like delirium). The report “Interim guidance for the appropriate support of people with dementia in the current COVID-19 pandemic scenario” was sent to 4,609 representatives of outpatient dementia care services. Additional videos and iconographic materials were released to improve the diffusion of the main contents (https://www.epicentro.iss.it/demenza/demenze-covid19-report-ISS-2020).

Conclusions:: The impact of the report will be assessed throughout the pandemic with dedicated initiatives.
Background and Aims:: There is a wide variety of viruses that can predispose to longitudinal-transvers myelitis in humans and COVID-19 seems to be no different. Here we would like to present the case of a 45-year-old male, COVID-19 convalescent, with family history of sclerosis multiplex. He was admitted to the Department of Neurology and Neuroimmunology in late October 2020 after being hospitalized on Internal Diseases ward due to urine congestion, constipation and progressive lower limbs palsy.

Methods:: A series of tests and imaging studies led to the diagnosis of longitudinal-transverse myelitis of undetermined cause. We run cerebrospinal fluid and serology tests to search for immune background, however we have not found any specific antibodies present nor any other typical cause. The patient denied any COVID-19 related symptoms in recent past, and he had no record of positive COVID-19 PCR test. We run another blood test to determine whether had he underwent COVID-19 infection asymptotically. The man turned out to be seropositive for anti-SARS-CoV2 and anti-SARS-CoV2 IgG antibodies that confirmed our suspicion. We introduced treatment with steroids after which neurologic symptoms subsided.

Results:: There are known cases of myelitis in COVID-19 patients and convalescents, however, there usually is a history of previously detected and symptomatic infection and myelitis onset begins between day 7-10 after first COVID-19 symptoms.

Conclusions:: In present era it would seem to be crucial to screen patients with myelitis for anti-SARS-CoV2 seropositivity.
THE RISK OF CORONAVIRUS DISEASE (COVID-19) TRANSMISSION TO HEALTH WORKERS IN THE NEUROLOGY MEDICAL SERVICE AT DR. CIPTO MANGUNKUSUMO NATIONAL HOSPITAL, JAKARTA

Ahmad Yanuar Safri, Riwanti Estiasari, Kartika Maharani, Astri Budikayanti, Ediva Pradiptaloka, Jovita Stephanie, Darma Imran, July Kumalati
University of Indonesia, Neurology, Jakarta, Indonesia

Background and Aims:: Background and Aims COVID-19 transmission in the hospital environment is a serious threat to the patients and health or non-healthcare workers. Previous research identified changes in patients' status to COVID-19 positive during the treatment period reached 10.06%; indicated the high risk of transmission, including in neurology treatment area. This study aims to identify COVID-19 risk factors in the neurology medical service of Cipto Mangunkusumo General Hospital.

Methods:: Methods Health workers and non-health workers in non-COVID 19 neurology medical services went through a serial serological examination of total COVID-19 antibodies (day 1 and 30) or PCR test if clinical manifestation was found. Demographic, clinical, dan risk factors were assessed using a questionnaire (day 0, 7, 14, 21,30). Identification of risk factors classified as internal and external, which assessed the activities and contact history within or outside the hospital.

Results:: Result Among 103 subjects, seven subjects are diagnosed as COVID-19 based on PCR or seroconversion in antibody test. The significant internal risk factor identified were worked in shift (p = 0.045; OR 1.12), ate together (p = 0.002; OR 18), contacted within ≤ 1 meter (p = 0.029 ; OR 1.125), and performed procedures that involved physical contact (p = 0.004; OR 1.17). The significant external risk factor was going to public places on weekends (p = 0.029; OR 1.125).
Conclusions: The main risk factor for transmission of COVID-19 in the neurology medical service of Cipto Mangunkusumo hospital is public spaces usage outside of health service hours, namely the habit of eating together.

<table>
<thead>
<tr>
<th>Internal Hospital Risk Factor</th>
<th>Changes in COVID-19 Status</th>
<th>P</th>
<th>OR (95%CI)</th>
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<td>Unit Location</td>
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<td>1.12 1.03-1.22</td>
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<td>Work Frequency</td>
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<tr>
<td>&gt;3 days/week</td>
<td>7</td>
<td>100</td>
<td></td>
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<tr>
<td>1-3 days/week</td>
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<td>14</td>
<td>0.002 15.206-157.1</td>
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<tr>
<td>Shift</td>
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<td>Non-Shift</td>
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<td>Eating Behaviour</td>
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<tr>
<td>Alone</td>
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<td>143</td>
<td>0.007 1.007-1.007</td>
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<tr>
<td>Together</td>
<td>6</td>
<td>857</td>
<td>1.00 1.00-1.00</td>
</tr>
<tr>
<td>In the open space</td>
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<td>143</td>
<td>0.007 1.007-1.007</td>
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<tr>
<td>In the closed space</td>
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<td>857</td>
<td>1.00 1.00-1.00</td>
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<td>Within the Same Room with COVID-19 Patient</td>
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<td>0.003 1.003-1.003</td>
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<td>Contact Distance with COVID-19 patient</td>
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<td>&lt;1 meter</td>
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<td>≤15 minutes</td>
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<td>Go to Public Space</td>
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<td>&gt;15 minutes</td>
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<td>Contact History with COVID-19 patient</td>
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A STUDY ON NEUROLOGICAL PROBLEMS ARISING DUE TO COVID-19

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EGC, Department Of Pharmacology, Mehsana, India

**Background and Aims::** The COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been predominantly a respiratory manifestation. Currently, with evolving literature, neurological signs are being increasingly recognized. Studies have reported that SARS-CoV-2 affects all aspects of the nervous system including the central nervous system (CNS), peripheral nervous system (PNS) and the muscular system as well. Not all patients have reverse transcription-polymerase chain reaction positive for the virus in the cerebrospinal fluid, and diagnosing the association of the virus with the myriad of neurological manifestations can be a challenge. It is important that clinicians have a high-index of suspicion for COVID-19 in patients presenting with new-onset neurological symptoms.

**Methods::** The neurological manifestations can broadly be categorized into CNS and PNS. The neurological manifestations are commonly observed in older age and critically ill patients. We are reporting a clinical data of 200 patients with COVID-19 over a three-week period showcasing neurological or psychiatric disease in Gujarat, India.

**Results::** Notably, cerebrovascular event in (46%) patients, ischaemic stroke in 57 (62%), intracerebral haemorrhages in nine (7%) and CNS vasculitis in one (<1%) patients were documented. This study also reported altered mental status in 31 per cent of patients, encephalopathy (13%) and neuropsychiatric diagnosis (18%).

**Conclusions::** The neurological manifestations in patients with COVID-19 are varied and can emerge standalone or during the clinical course. Upholding a high-index of suspicion for COVID-19 in patients presenting with new-onset neurological symptoms will expedite an early diagnosis. Further studies are desired to unravel these varied neurological manifestations, treatment in COVID-19 patient.
COVID-19 IN PATIENTS WITH MYASTHENIA GRAVIS: WHICH PROGNOSIS?

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Background and Aims:: Coronavirus disease 2019 (COVID-19) is now the major public health concern worldwide. It can cause neurological complications and increase risk of exacerbations of chronic neurological disorders.

Methods:: We report a series of patients with myasthenia gravis who developed COVID-19 and referred to the neurology department of the Military Hospital of Tunis. Clinical characteristics and outcome of these patients are described.

Results:: Four patients with previously stable Myasthénia Gravis, had myasthenic exacerbation and were hospitalized in our department. One patient presented diplopia and two patients had dysphagia and limb weakness. One of them developed hypoxemic respiratory failure and required Intensive care unit admission and intubation. Three patients were treated with intravenous immunoglobuline. Increasing steroid doses was necessary in two cases. The outcome was favorable for all patients.

Conclusions:: Clinical course and outcome in patients with Myasthenia gravis and COVID-19 are variable. Early treatment is necessary in order to improve the prognosis of these patients.
COVID-19 IN PATIENTS WITH MYASTHENIA GRAVIS

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Background and Aims:: Coronavirus disease 2019 (COVID-19) has rapidly become a global pandemic, but little is known about its potential impact on patients with myasthenia gravis (MG).

Methods:: We studied the impact of COVID-19 infection on the clinical course of three hospitalized patients with acquired myasthenia gravis.

Results:: The first patient with previously stable MG had severe pneumonia. He required intubation for hypoxemic respiratory failure. He died within 48 hours. Whereas the two others required significant supplemental oxygen (high-concentration mask and non-invasive mask ventilation alternately). They were treated with cefotaxim, fluoroquinolone and then with tazocilline and received intravenous immunoglobulin, leading to full recovery.

Conclusions:: Our findings suggest that COVID 19 give rise to severe acute respiratory illness in patients with MG. They are at greater risk of poor prognosis.
**Background and Aims:** The World Health Organization (WHO) declared the coronavirus, a severe respiratory distress syndrome, Sars Cov 2 a global health emergency because of its rapidly transmissible nature, increasing mortality rate. Long-term sequelae of SARS-CoV-2 infection have become increasingly recognized and need huge effort to prevent and care.

**Methods:** We set up a 3 months follow-up of 160 patients, 82 women and 78 men, admitted in the Emergency Medicine Covid from October 2020 to March 2021. The mean age was 60. Asthenia, fever, cough myalgia, headache, anosmia, and ageusia are the most common primary symptoms.

**Results:** All the patients performed blood test, neuroimaging, respiratory and neurological assessment. We noticed a decrease in the laboratory findings inflammatory response. The Chest CT showed significant pulmonary fibrosis in 70 patients. 80 patients had a neuropsychological consequences, associated with depression, sleep impairment, anxiety, loss of memory and concentration, ageusia, anosmia, headache and global asthenia. Patients with pre-existent disease experienced a worsening, especially those with cognitive decline.

**Conclusions:** Currently, as we are still experiencing the pandemic and its effects, it is too early to describe the full clinical picture of post Covid syndrome. We need for more long-term clinical follow-up data to prevent long-term sequelae and Post Covid Neurological Syndromes. We need ongoing neurological cognitive and affective monitoring of all cases of Covid 19 to formulate relevant prevention and intervention strategies. Finally, the economic impact of this disorder, together with patient care, must be worked out in advance.
THE AFTER-COVID SYNDROME: A SURVEY OF POSTTRAUMATIC STRESS SYNDROME IN 111 RESIDENTS IN MOROCCO

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¹Mohammed VI University Medical Center, Marakesh, Neurology, Marrakesh, Morocco, ²Mohammed VI University Medical Center, Marakesh, Psychiatry, Marrakesh, Morocco, ³Mohammed VI University Medical Center, Marrakesh, Neurology, MARRAKECH, Morocco

Background and Aims:: The aim of this study was to investigate the incidence of symptoms of posttraumatic stress in a survey of infected and non-infected respondents in Morocco, and determine the risk factors.

Methods:: An online survey was conducted in 111 respondents and required them filling out a posttraumatic stress screening form.

Results:: Of 111 respondents, (average age: 24.3 ± 3.7 years; male-to-female ratio: 0.6), 18.9% reported having been infected by the Covid-19 virus. 64.5% said they had an infected close relation; 26.1% report knowing a close person who passed away from Covid. 55% frequently suspected being infected. The majority of respondents (56.8%) never got tested. Overall, 64.5% respondents met the criteria for possible posttraumatic stress syndrome. 42.3% respondents reported having had intrusions about experiences during the pandemic, 40.5% reported avoiding things or situations that reminded them of past Covid experiences, 38.7% reported having negative moods and thoughts concerning Covid, 29.7% reported having sleep or some other behavioral disturbances. Females reported relatively more symptoms than males (82.3% versus 69.0%) but the difference did not reach statistical significance (p = 0.092). Factors associated with symptoms were whether one was a Moroccan or a foreigner (p= 0.026), whether one knew a person who died from Covid infection or not (p= 0.026), or whether one was infected by Covid or not (p= 0.002).

Conclusions:: Posttraumatic stress syndrome is a frequent sequela of the Covid-19 pandemic and should be recognized as such by all in order for people to seek help to ensure a smooth return to normal life again.
Background and Aims:: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is focusing primarily on respiratory complications. A comprehensive review of the neurological disorders reported during the current COVID-19 pandemic demonstrates that infection affects the central nervous system (CNS), the peripheral nervous system (PNS) and the muscle.

Methods:: In this retrospective, observational study, we enrolled 748 patients, with laboratory confirmed diagnosis of severe acute respiratory syndrome from coronavirus 2 (SARS-CoV-2) infection. Data were collected from March to May 2020 and from October to April 2021 and were extracted from electronic medical records. Neurological symptoms included central nervous system headache, dizziness, impaired consciousness, acute cerebrovascular disease, and epilepsy, peripheral nervous system symptoms, hypogeusia, hyposmia, hyposia, and neuralgia, and skeletal muscle injury. Data of all neurological symptoms were checked by a multidisciplinary team.

Results:: 814 patients admitted to the Urgency Medicine ward 284 were severe and 530 were nonsevere patients. Severe patients were older, and showed less typical symptoms. 633, 78% patients had neurolologic manifestations hypoageusia, hyposmia, neuralgia, headache, 29 patients had stroke, 2 Myastenic syndrome, 2 Guillaume Barre, 1 encephalitis

Conclusions:: The SARS-CoV-2 pandemic has implications for all areas of medicine. SARS-CoV-2 infection is associated with an increased incidence of neurological manifestations. Involvement of the nervous system carries a poor prognosis. The pathobiology of these neuroinvasive viruses is still incompletely known, and it is therefore important to explore the impact of CoV infections on the nervous system.
COVID-19 PRESENTING AS NEUROLOGICAL MANIFESTATIONS, RARE CASES IN NEUROLOGICAL DEPARTMENT.

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Social security organization, Mashhad, Iran, Neurological, Mashhad, Iran

Background and Aims:: Coronavirus disease 2019 caused by severe acute respiratory syndrome coronavirus 2 infection, is associated with coagulopathy causing venous and arterial thrombosis. SARS-CoV-2 infection is linked to a prothrombotic state causing venous and arterial thromboembolism and elevated D-dimer levels.

Methods:: A 50-year-old male taking warfarin for AF, presented 2 days after COVID-19 symptom onset (ARDS) with acute confusion, incoordination and drowsiness; GG pattern was reported in HRCT. CT brain confirmed acute large left cerebellar and left occipital infarcts. D-dimer was increased and the (INR) 3.6 at the time of stroke symptoms. A 67-year-old man with hypertension, presented with dysarthria and left hemiparesis. MRI brain showed an acute right MCA infarct. D-dimer was 27,000µg/L. A days following admission, he developed respiratory symptoms. RT-PCR confirmed SARS-CoV-2 infection.

Results:: The 45-year-old patient had severe muscle pain and had a mild cough and low grade fever. Groud glass was reported in HRCT tests and mild lymphopenic but increased enzyme creatinine kinase levels (4500) were significant improved. It lasted for two consecutive weeks. A 25-year-old previously healthy female was admitted with generalized tonic-clonic seizure in our hospital. The patient complained of dry cough 2 days before the admission. Brain MRI was normal and chest CT revealed focal ground-glass opacities. The respiratory specimen was positive for COVID-19 using real-time PCR assay. The symptoms of the patient improved with anticonvulsive and antiviral medications.

Conclusions:: Severe COVID-19 is associated with proinflammatory cytokines which induce endothelial and mononuclear cell activation with expression of tissue factor leading to coagulation activation and thrombin generation.
NEUROLOGICAL PRESENTATION OF COVID-19: EXPERIENCE FROM A TERTIARY CARE HOSPITAL OF BANGLADESH

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¹BIRDEM General Hospital, Neurology, Dhaka, Bangladesh, ²Dhaka Medical College, Hematology, Dhaka, Bangladesh

Background and Aims:: Neurological manifestations of COVID-19 are being recognized day by day although predominant presentation is of respiratory illness. Understanding of impact of the virus on nervous system is important for selection and evolution of treatment now and in the future. The aim of the study was to describe the manifestations of COVID-19 affecting nervous system in a tertiary care hospital of Bangladesh

Methods:: This cross-sectional study was carried out in Department of Neurology, (BIRDEM) General Hospital from March, 2020 to October, 2020. Total forty patients who were admitted under neurology department were included in the study. Clinical syndromes associated with COVID-19 were classified broadly as a cerebrovascular event, altered mental status and peripheral nervous system disorders.

Results:: Median age of the patients was 58.6 years (range 22–73). Among those, 26(65%) were male and 14(35%) were female. Twenty two (55%) of 40 patients presented with cerebrovascular event, of whom 15 (68%) had an ischaemic stroke, 5 (23%) an intracerebral haemorrhage. 2(9%) patients were diagnosed as cerebral venous sinus thrombosis. Apart from cerebrovascular events, 14 (35%) of 40 patients presented with altered mental status, comprising 9 (64%) patients with unspecified encephalopathy and 5 (36%) patients with encephalitis. Four (10%) patients were diagnosed as peripheral nervous system disorder among those 2(50%) as Guillain-Barré syndrome (GBS) and 2(50%) as Bell’s palsy.

Conclusions:: We have found cerebrovascular disease, encephalopathy and peripheral nervous system disorder as presentation of COVID-19 in our study. Further nationwide study is needed to quantify the association and disease burden.
CEREBRAL VENOUS SINUS THROMBOSIS AND CORONA VIRUS INFECTION (COVID-19): A MULTICENTER ASIAN STUDY

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Aga Khan University, Stadium Road, Karachi., Neurophysiology Department, Consulting Clinic-1, Karachi, Pakistan

Background and Aims: Coronavirus disease 2019 (COVID-19) has an increased propensity for systemic hypercoagulability and thromboembolism. An increase in cerebrovascular diseases has also been reported among these patients. The objective of the present study is to identify risk factors, presentation, and outcome of CVST in COVID-19 patients.

Methods: It is a multicenter and multinational prospective observational study. Ten centers in four countries, Pakistan, Egypt, Singapore, and the United Arab Emirates, participated in the study that included patients (aged > 18 years) with symptomatic CVST and recent COVID-19 infection.

Results: Twenty patients (70% men) were included. Mean age was 42.4 years. Headache (85%) and seizures (65%) were the common neurological features with a mean admission GCS of 13. Respiratory symptoms were absent in 45% of the patients. The most common MRI finding was ischemia (65%) followed by hemorrhage (20%). Superior sagittal sinus (65%) was the most common site for thrombosis. Acute inflammatory markers were raised with abnormal serum D-dimer (87.5%), erythrocyte sedimentation rate (69%), and C-reactive protein (47%) levels. Homocysteine was elevated in half of the cases. Mortality rate was high (20%). A good functional outcome was seen in the surviving patients with a mean discharge mRS score of 1.3.

Conclusions: COVID-19 patients are at high risk for CVST secondary to the high incidence of systemic thromboembolism. A low threshold for brain imaging should be kept for COVID-19 patients presenting with headache or seizures. Presuming a high prevalence of asymptomatic cases, all patients with newly diagnosed CVST should undergo testing for COVID-19 infection.
KNOWLEDGE, ATTITUDES, AND IMPACT OF COVID-19 PANDEMIC AMONG NEUROLOGY PATIENTS IN JORDAN: A CROSS-SECTIONAL STUDY

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¹Yarmouk University Faculty of Medicine, Neuroscience, Irbid, Jordan, ²Princess Basma Teaching Hospital, Neurology, Irbid, Jordan, ³King Abdullah University Hospital, Neuroscience, Irbid, Jordan, ⁴Jordan University of Science and Technology, Public Health And Community Medicine, Irbid, Jordan

Background and Aims:: The impacts of COVID-19 pandemic on health services offered to patients with non-communicable diseases, including chronic neurological illnesses, are diverse and universal. This study aims to investigate these impacts on neurology patients in Jordan and assess their knowledge and attitudes towards the pandemic.

Methods:: We administered a paper-based, self-reported survey to neurology outpatients at a community hospital in the north of Jordan. The survey included demographics as well as disease-specific questions related to multiple sclerosis, epilepsy and migraine or tension headache. Knowledge and attitude towards the COVID-19 pandemic were also assessed.

Results:: Most respondents had positive attitudes towards COVID-19 pandemic, with 96% reporting they believed in the seriousness of the pandemic and adhered to prevention measures. Nearly 97% resorted to the internet and media outlets for medical information about the pandemic. About one in five clinic visitors had their appointments delayed due to interruption of health services. A similar portion of patients with MS, epilepsy and migraine or tension headache reported medication interruptions during the pandemic. One in two patients reported new events or worsening illness since the start of the pandemic, and sleep disturbances were reported by nearly one in three patients who had epilepsy or headache.

Conclusions:: Most surveyed neurology patients had positive attitudes towards COVID-19 pandemic. Also, the negative impacts of the pandemic on patients with neurological illnesses in Jordan were evident and diverse.
NEUROLOGICAL SYMPTOMS IN PATIENTS WITH COVID-19 AS MANIFESTATION OF SEVERITY AND PROGNOSIS, THE CASE OF ANOSMIA AND DYSGEUSIA

Luis Del Carpio-Orantes¹, Sergio García-Méndez², Ishar Solís-Sánchez¹, Miguel Arnulfo Perfecto-Arroyo³, Nancy Patricia Moreno-Aldama³, Jesús Salvador Sánchez-Díaz¹
¹Instituto Mexicano del Seguro Social, Internal Medicine, Veracruz, Mexico, ²Hospital Regional de Alta Especialidad de Oaxaca, Internal Medicine, Oaxaca, Mexico, ³Instituto Mexicano del Seguro Social, Neurology, Veracruz, Mexico

Background and Aims:: With the COVID-19 pandemic, attempts have been made to use various tools for prognostic purposes, however, the clinical manifestations that can act positively or negatively have not been taken into account.

Methods:: Descriptive and retrospective study carried out from April to June 2020 in Veracruz, Mexico, which analyzes adult patients with a diagnosis of COVID-19 pneumonia confirmed, in which the most prevalent neurological symptoms are evaluated, in order to find symptoms that act as severity and prognosis factors.

Results:: We analyzed 100 patients with COVID-19 pneumonia; 46 women and 54 men, with a mean age of 49.4 (± 19.3). The most frequent neurological symptoms were: headache (83%), anosmia (75%), dysgeusia (75%), myalgia (68%) and somnolence (50%). Somnolence and anosmia were more frequent in severe pneumonia than in mild pneumonia [(67.4 VS 35.2%; p = 0.002) and (84.8 VS 66.7%; p = 0.041); respectively]. By simple and multiple logistic regression analysis, it was found that the neurological manifestations associated with severe pneumonia, risk of intubation and death were: anosmia, somnolence, encephalopathy and age over 70 years, in contrast to neurological manifestations with a protective effect against severe pneumonia, intubation and death were: dysgeusia and age under 40 years.
Odds Ratios (OR) of the neurological variables for the development of severe pneumonia in patients with COVID-19.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Simple logistic regression</th>
<th>Multiple logistic regression</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>Age &lt;40 yo</td>
<td>0.10</td>
<td>0.03 – 0.28</td>
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<tr>
<td>Age 40 - 59 yo</td>
<td>1.39</td>
<td>0.49 – 3.98</td>
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<td>Age 60 - 69 yo</td>
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<td>Age ≥70 yo</td>
<td>11.37</td>
<td>2.42 – 53.36</td>
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<tr>
<td>Female genre</td>
<td>1.87</td>
<td>0.84 – 4.15</td>
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<td>Headache</td>
<td>0.71</td>
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<td>Drowsiness</td>
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<td>Dizziness or vertigo</td>
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<td>0.53 – 2.96</td>
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<tr>
<td>Encephalopathy</td>
<td>5.04</td>
<td>0.54 – 46.86</td>
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<tr>
<td>Delirium</td>
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<td>0.21 – 27.46</td>
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<td>Convulsives crisis</td>
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<td>0.05 – 6.58</td>
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<tr>
<td>Cerebral stroke</td>
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<td>Dysgeusia</td>
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<tr>
<td>Myopathy or hypotrophy</td>
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<td>0.07 – 19.37</td>
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* Multiple logistic regression analysis performed with Wald’s step-forward method.
<table>
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<th>Variable</th>
<th>OR</th>
<th>Simple logistic regression</th>
<th>Multiple logistic regression</th>
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<td>Encephalopathy</td>
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<tr>
<td>Cerebral stroke</td>
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<td>0.00 – 0.00</td>
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<td>Dysgeusia</td>
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<td>Distal paresthesias</td>
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<td>0.17 – 3.05</td>
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<tr>
<td>Myalgia</td>
<td>1.36</td>
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<tr>
<td>Myopathy or hypotrophy</td>
<td>1.80</td>
<td>0.10 – 29.67</td>
<td>0.498</td>
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* Multiple logistic regression analysis performed with Wald’s step-forward method.
Conclusions:: The presence of anosmia, drowsiness, and encephalopathy is associated with greater severity of the disease and with intubation requirements and death, while dysgeusia has a protective effect against severity, intubation and death associated, acting as prognostic factors and severity of the disease.
SUBCLINICAL MYOPATHIC CHANGES IN COVID 19

Davide Villa1, Gianluca Ardolino2, Linda Borellini2, Filippo Cogiamanian2, Maurizio Vergari2, Sergio Barbieri2
1Foundation IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Centro Dino Ferrari, University of Milan, Milan, Italy, Neurophysiology-neurology, Milan, Italy, 2Foundation IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan, Italy, U.o. Neurophysiology, Milan, Italy

Background and Aims:: Coronavirus disease 2019 (Covid 19) is associated to neuromuscular symptoms in up to 10.7% of hospitalized patients. The prevalence and the characteristics of intensive care unit acquired weakness (ICUAW) in patients affected by Covid 19 have been extensively assessed, although no distinctive pattern was found. ICUAW has been described as a potential confounding factor during the identification of severe acute respiratory syndrome coronavirus 1-related myopathy. In order not to incur this potential bias, we focused on a subset of non-severe cases. Our aim was to precisely assess the extent of primary neuromuscular involvement with neurophysiological investigation in Covid 19 patients.

Methods:: From April through May 2020 a total of 70 patients were hospitalized in the Internal Medicine Ward of the Fondazione IRCCS Ospedale Maggiore Policlinico in Milan, Italy. After excluding patients who underwent invasive ventilation and steroid treatment, 12 patients were evaluated. Neurological examination, nerve conduction studies (NCS) and concentric-needle electromyography (EMG) were performed.

Results::
While nerve conduction studies were unremarkable, needle electromyography showed myopathic changes in 6 out of 12 subjects. All patients were asymptomatic for muscular involvement. Clinical features and laboratory findings did not show relevant differences between patients with and without myopathic changes.

**Conclusions:** Our data show that in SARS-CoV-2 infection muscular involvement can occur despite the absence of clinical signs or symptoms and should be considered part of the disease spectrum. The application of muscle biopsy to unravel the mechanisms of myofiber damage on tissue specimens could help to clarify the pathogenesis and the treatment response of coronavirus-mediated injury.
Background and Aims:: There is emerging evidence that COVID-19 can trigger thrombosis because of a hypercoagulable state, including large vessel occlusion ischemic strokes. Bi-hemispheric ischemic stroke is uncommon and is thought to indicate an embolic source.

Methods:: We performed a retrospective cohort study at a quaternary academic medical center between March 1st and April 30th, 2020. We identified all patients with laboratory-confirmed SARS-CoV-2 infection who presented with simultaneous bi-hemispheric ischemic strokes.

Results:: Of 637 COVID-19 admissions during the two-month period, 13 had a diagnosis of acute ischemic stroke, including 5 who developed with bi-hemispheric cerebral infarction. Three (60%) were female, median age was 54 (range 41-67), and all five were being managed for severe COVID-19 related pneumonia complicated by acute kidney injury and liver failure before the diagnosis of cerebral infarction was established. Five presented with elevated ferritin, lactate dehydrogenase, and interleukin-6 (IL-6) levels, and four had lymphopenia and elevated D-dimer levels. All patients underwent neuroimaging with CT for persistent depressed mentation, with or without a focal neurologic deficit, demonstrating multifocal ischemic strokes with bi-hemispheric involvement. Outcome was poor in all patients: we discharged two to a rehabilitation facility with moderate-to-severe disability, and three (60%) patients died.

Conclusions:: Stroke is implicated in SARS-CoV-2 infection. Multifocal ischemic strokes with bi-hemispheric involvement should be considered in COVID-19 patients with severe infection and poor neurologic status and may be associated with poor outcomes.
THE EFFECT OF COVID-19 PANDEMIC ON PATIENTS WITH NEUROLOGICAL DISORDERS CONSULTING TELEMEDICINE OPD

Ruchika Tandon, Sushant Aildasani
Sanjay Gandhi Postgraduate Institute of Medical Sciences, Neurology, Lucknow, India

Background and Aims:: Electronic or telemedicine OPDs (e-OPDs) are being utilized for providing outpatient care to neurology patients during Severe Acute Respiratory Syndrome Corona virus-2 (SARS COV-2) or COVID-19 pandemic.

Methods:: We assessed knowledge, attitude and practices of 300 neurological e-OPD patients with regard to COVID-19 pandemic and perceived effect of this pandemic on their neurological problems via questionnaire.

Results:: Out of 300 patients (60% males), people between 20 and 40 years of age (35.3%) and those with seizures (28%) and strokes (17.3%) were most frequent visitors. Though 96% of all individuals were aware of the COVID-19 disease, only 34% patients fully followed disease preventive measures. Maximum numbers of patients were aware of airborne (54%) route of disease transmission and greatest number of people used face mask (88%). Follow up patients (71.3%) most frequently utilized e-OPDs and 56.1% of these patients contacted earlier than scheduled visits. 17.3% felt that there was a delay in emergency visit. The commonest reason for delay in emergencies as well as in follow-ups was government restriction (53.8% and 40.2%, respectively) and most common reason for arrival was regular follow up in 55.1% and reasons other than emergency or insistence from caregivers in 46.7% first visits. The e-OPD interaction satisfied most of the patients as well as doctors.

Conclusions:: In spite of good awareness of disease, very few patients were fully following COVID-related precautions. Fear of Government was motivating factor for most patients. There was a delay in very few neurological emergencies. Impact of COVID-related restrictions on neurological patients, was not significant.
ADEM POST SARS-COV-2 INFECTION IN A PAEDIATRIC PATIENT WITH FISHER EVANS SYNDROME

Maria Laura Manzo, Cristina Galati, Cristina Gallo, Giuseppe Santangelo, Antonio Marino, Fulvio Guccione, Vincenzo Raielli, Renata Pitino
University of Palermo, Child Neuropsychiatry School, Palermo, Italy

Background and Aims:: Introduction: Sars-CoV-2 is a single-strained RNA virus belonging to Coronaviridae's family. In paediatric age the majority of patients are asymptomatic, however several neurological manifestations associated with Sars-CoV-2 infection have been detected in a percentage of cases ranging from 17.3% to 36.4%. Acute Disseminated Encephalomyelitis (ADEM) has been recently included among the potential complications of Sars-Cov2 infection. The available data regarding paediatric patient show only one case.

Methods:: Case report: We present a case regarding a six-year-old child suffering from Fisher Evans Syndrome treated with Sirolimus and Thalidomide therapy and affected by Sars-CoV-2 infection.

Results:: Case report: We present a case regarding a six-year-old patient suffering from Fisher Evans Syndrome who was given Sirolimus and Thalidomide therapy. After ten days since the first positive nasopharyngeal swab for Sars-CoV-2, in which he had no symptoms, he presented an episode of generalized tonic-clonic seizure with spontaneous resolution. The patient underwent MRI which showed the typical picture of Acute Disseminated Encephalomyelitis. His clinical course was favourable, with a good response to cortisone therapy and a progressive improvement of the neuroradiological and electroencephalographic picture.

Conclusions:: according to our knowledge, this is the second case of an Acute Disseminated Encephalomyelitis following SARS-CoV-2 infection in a paediatric patient, characterized by monosymptomatic onset, in which the immunosuppressive therapy practiced for the Fisher Evans Syndrome has probably contributed to a favourable evolution of ADEM, in contrast to other case described in the literature.
Background and Aims:: Coronavirus Disease 19 (COVID-19) was declared a pandemic by the World Health Organization (WHO) in March 2020. Since the outbreak, neuropsychiatric presentations such as delirium and confusion have been developing. Our aim is to describe the differences between inpatients cursing with Acute Confusional Syndrome (ACS) with and without COVID-19 pneumonia.

Methods:: This is an observational-descriptive study. All patients attended by the liaison psychiatry service of Hospital del Mar, between February and April 2020, with ACS diagnosis were included. The sample was divided in 2 groups (with and without COVID-19 pneumonia). Sociodemographic and clinical variables including sex, age, admission duration, previous somatic or psychiatric history and risk factors associated with ACS were compared. Chi-square and U Mann Whitney tests were used for comparisons.

Results:: The total sample was 62 patients. 43.5% were women with a mean age of 71.7 (SD 11.3). Covid pneumonia group mean age was lower (69, SD=8.4) (p=0.033) Covid pneumonia group included 26 patients. There were significant differences between Covid pneumonia group and ACS in relation to a previous diagnosis of: Ischemic Heart Disease (p=0.007), Heart Failure (p=0.029) and Nephropathy (p=0.022). Risk factors associated with ACS such as cognitive impairment or hypoxemia were compared. There was a higher percentage of Hypoxemia in Covid pneumonia patients (p<0.001)

Conclusions:: In this sample, patients with ACS and Covid pneumonia had a bigger rate of hypoxemia and a previous history of Ischemic Heart Disease, Heart Failure and Nephropathy compared to the rest of ACS patients. More studies would be necessary to assess the significance.
Background and Aims:: Initially barely affected by the Covid 19, the African continent suffered a second violent wave this winter. Neurological manifestations worldwide are increasingly reported, dominated by encephalitis, stroke and polyradiculoneuritis. We report the Senegalese experience of NeuroCovid through a series of 9 patients.

Methods:: This is a prospective study of patients hospitalized in the neurology department of Fann. Were included patients who had neurological manifestations during or following an COVID-19 infection defined by a positive PCR or a recent infection with ELISA serology or typical chest imaging.

Results:: We collected 9 patients (6 men and 3 women), aged 7 to 80 years. Diagnoses were: 3 encephalitis, 4 polyradiculoneuritis, 1 hemorrhagic stroke and 1 chorea. 4 patients had comorbidities. The delay for neurological signs appearance was 11.1 days. A nasal swab was positive on 5/8 patients. Antibodies were found in all 3 negative patients. The LCR study showed hyperproteinorrachia in 7/9 patients. 5 patients underwent CT chest scan, showing ground glass opacities. Brain imaging was normal in 3 and pathological in 2, showing a parietal temporo hematom
in one and mesencephalic and parietal hypersignal in the other.
50% of patients with polyradiculoneuritis had an ENMG that showed an AIDP. One patient had an electroencephalogram that showed an overall slowing of the pattern with diffuse pseudoperiodic complexes.
Evolution was good for 6 patients but we noticed 3 deaths.

**Conclusions:** Neurological manifestations most often occur in post-infection. The creation of a multidisciplinary team will allow a better understanding of the sequelas of patients with COVID-19.
VISUAL HALLUCINATION IN DELIRIUM ASSOCIATED CORONAVIRUS DISEASE 2019 (COVID-19): A CASE SERIES

Rocksy Fransisca V. Situmeang¹, Aristo Pangestu²
¹Siloam Hospital Lippo Village, Memory Clinic, Neurology Department, Tangerang, Indonesia, ²Siloam Hospital Lippo Village, Neurology, Tangerang, Indonesia

Background and Aims:: The increasing number of COVID-19 confirmed cases is also accompanied by an increasing number of reports of atypical symptoms, one of which is delirium. Visual hallucinations as a symptom of delirium are rarely reported in COVID-19.

Methods:: We report 3 COVID-19 confirmed patients with symptoms of delirium accompanied by visual hallucinations.

Results:: All patients were male, 2 were elderly patients (66 and 72 years) and 1 patient was relatively younger (29 years). All patients denied the use of substance abuse and do not have neuropsychiatric comorbidities. Complex visual hallucinations were found in 2 patients and 1 mixed visual hallucination was found in 1 patient. The visual hallucination features found are typical of delirium. We proposed two mechanisms for visual hallucinations in delirium associated COVID-19, namely the involvement of the reticular activating system and dysregulation of neurotransmitters, especially dopamine.

Conclusions:: Visual hallucinations can be an atypical presentation of delirium associated COVID-19 in patients without comorbid of neuropsychiatric illness. Further research is needed to determine the impact of outcome and severity as well as the pathomechanisms for visual hallucinations in delirium associated COVID-19.
POOR OUTCOME OF MYASTHENIA GRAVIS IN COVID-19: A TERTIARY PUBLIC HOSPITAL EXPERIENCE

Godard Artajos, Marissa Ong
EAST AVENUE MEDICAL CENTER, Neurosciences, QUEZON CITY, Philippines

Background and Aims:: The COVID-19 Pandemic has caused a great concern worldwide. Myasthenia Gravis is known to be a challenging disease on its own. Most of the time the management of MG would include immunosuppression which could lead us to think that these patients may be at higher risk of contracting an infection or experience severe manifestations of COVID-19. [3] Current data might be biased toward poor outcome of patients with myasthenia gravis with COVID-19; more likely to be hospitalized, have disease exacerbations, and have a higher risk for mortality than the general population with COVID-19.

Methods:: This case series will present how a concurrent COVID 19 infection affected the outcomes of patients with Myasthenia gravis.

Results:: In our observation, other factors that may contribute to a poorer outcome are pregnancy and presence of other co-morbidities. The first case was pregnant. The second patient was undergoing treatment for pulmonary tuberculosis. The third case had more than two chronic illnesses and risk factors. In our setting, additional factors like accessibility to a health facility, proper patient education and availability of medications and equipment need to be considered. Despite improvement of myasthenic symptoms, there was progression of respiratory infection leading to poor outcome of the patients.
Conclusions:: For third-world countries like the Philippines, patient education and monitoring is very important for the prevention of hospitalization due to myasthenic crisis or COVID-19 infection. Further studies are recommended to establish the effects of pregnancy and other co-morbidities in the poor outcome of MG in COVID-19.
A CASE OF COVID-19 ENCEPHALITIS WITH ANTI-GFAP ANTIBODY-POSITIVE MENINGOENCEPHALOMYELITIS

Fan Cheng, Ker Tang  
Hull University Teaching Hospitals NHS Trust, Department Of Neurology, Kingston upon Hull, United Kingdom

**Background and Aims::** Neurological manifestations are increasingly recognised in COVID-19, caused by SARS-CoV-2. Anti-glial fibrillary acidic protein (GFAP) antibody (Ab)-mediated astrocytopathy can have parainfectious aetiologies.

**Methods::** We describe a patient with COVID-19 and adenovirus encephalitis preceding anti-GFAP meningoencephalomyelitis.

**Results::** A woman, 49, was admitted with headache, fever and positive SARS-CoV-2 nasal PCR. Over 72-hours, she developed drowsiness and confusion. CT head was normal. Cerebrospinal fluid (CSF) showed leukocyte 28/mm^3, protein 0.8g/dL and glucose 2.2mmol/L. She started empirical intravenous aciclovir and cefotaxime. MRI brain following improved agitation demonstrated right temporal T2 hyperintensities. On Day 10, CSF returned positive SARS-CoV-2 and adenovirus PCR (HSV, VZV, enterovirus PCR and microbial culture negative). COVID-19 and adenovirus encephalitis was diagnosed. 5-days dexamethasone and 14-days total aciclovir were given with clinical improvement. However, on Day 20, she developed new quadriparesis, myoclonus and fluctuating consciousness. Repeat MRI revealed new right temporal and parietal T2 hyperintensities, patchy enhancing cord lesions, and cauda equina and conus medullaris meningeal enhancement. Repeat CSF showed leukocyte 185/mm^3 (90% lymphocytes), protein 1.9g/dL, glucose 1.3mmol/L, with negative SARS-CoV-2 and adenovirus PCR. Serum and CSF anti-GFAP Ab were positive (titres: 1:128 and 1:64). Other autoimmune encephalitis/paraneoplastic/connective-tissue Abs and infective/malignancy screens were negative. After 5-days high-dose methylprednisolone with steroid taper, power and cognition began improving. CSF parameters and meningeal enhancement resolved when repeated after 1-month. She started mycophenolate, further improving at 3-months follow-up. .
Conclusions:: We report the first case of COVID-19 encephalitis preceding anti-GFAP meningoencephalomyelitis, supported by characteristic imaging-findings and steroid-responsiveness. We postulate COVID-19 and adenoviral infections immunologically precipitated anti-GFAP astrocytopathy.
COVID-19 INFECTION WITH ANTI-BASAL GANGLIA ANTIBODY-POSITIVE MOVEMENT DISORDERS AND PRESENCE OF SARS-COV-2 IN CEREBROSPINAL FLUID

Fan Cheng, Ker Tang
Hull University Teaching Hospitals NHS Trust, Department Of Neurology, Kingston upon Hull, United Kingdom

Background and Aims:: Movement disorders have been reported in COVID-19 infection, although underlying mechanisms are poorly-defined.

Methods:: We describe a case of COVID-19 with reversible myoclonus, dystonia and Parkinsonism associated with positive anti-basal ganglia antibodies (ABGA) and SARS-CoV-2 in cerebrospinal fluid (CSF), improving post-immunotherapy.

Results:: A man, 42, was admitted with cough, fever and positive SARS-CoV-2 nasal PCR without desaturation. Symptoms improved with supportive management. On Day 5, he developed jaw and faciobrachial myoclonus with involuntary sudden brief jaw, face and upper limbs jerks without seizure markers. He had no Parkinsonism at this point. Septic, metabolic, toxic and hypoxic causes were excluded. MRI head and electroencephalogram were unremarkable. Myoclonus continued daily despite multiple anti-epileptics. He developed gradual progressive cervical, bilateral hand and laryngeal dystonia from Day 9. Repeat MRI showed bilateral caudate and putamen T2 hyperintensities. CSF showed leukocyte 8/mm^3, protein 0.9g/dL, glucose 3.1mmol/L and negative viral PCR including SARS-CoV-2. Myoclonus and dystonia continued. Over the next 2-weeks, he developed bilateral bradykinesia and rigidity. DaTscan showed bilaterally reduced striatal tracer-uptake. Repeat CSF showed leukocyte 17/mm^3, protein 0.8g/dL, glucose 2.5mmol/L and positive SARS-CoV-2 PCR. Serum ABGA was positive. Anti-DNaseB, anti-Streptolysin-O, other encephalitis/paraneoplastic antibodies, metabolic/heavy-metal/malignancy screen, and Parkinsonism/dystonia genetic panel were negative. Given ABGA-positivity and mild CSF inflammation, he received high-dose methylprednisolone and, subsequently, intravenous immunoglobulin. Myoclonus, dystonia and Parkinsonism resolved over 5-months.
Conclusions: We report the first case of COVID-19 with ABGA-positive movement disorders and CSF SARS-CoV-2 presence, without hypoxia, suggesting cerebral entry of SARS-CoV-2 could induce movement disorders by precipitating ABGA-positive autoimmune encephalitis, which improves post-immunotherapy.
PHANTOMSIA AS A RARE NEUROLOGICAL MANIFESTATION IN PATIENT INFECTED WITH COVID-19: A CASE REPORT

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Universitas Brawijaya, Neurology, Malang, Indonesia

Background and Aims:: SARS-CoV-2 is a new strain of coronavirus, responsible for respiratory illness known as the COVID-19 pandemic, which has spread to several countries worldwide. Numerous otolaryngologists reported sudden event of anosmia or hyposmia as one of the symptoms of COVID-19 disease. Phantosmia often undetected because it only diagnosed through the patient's history. The diagnosis often missed because these symptoms were not specific.

Methods:: Man, 39-years old, presented with a 7-day history of chill and fever of unknown cause with no other symptoms, nor had a history of travels abroad. Rapid Test SARS Antibody examination was negative on the fourth day after his fever symptom with laboratory result was leukocytopenia and slight thrombocytopenia and diagnosed as Dengue fever. The chest x-ray examination result is pneumonia, which performs after 7-days of fever and after 1-day of dry cough. The fever's symptoms did not resolve even though he had fluid therapy and antibiotics. He began to complain about olfactory hallucination seven days from his fever symptom, which he always smelled of bitter medicine, and complained about shortness of breath, especially when he was doing activity even just for walking. His nasopharyngeal and oropharyngeal swab after ten days of the symptoms was positive.

Results:: His symptom of fever, dry cough, and olfactory hallucination wholly resolved after two weeks since initial symptoms without taking any specific medication.

Conclusions:: There are many other diseases has symptom like COVID-19. Here, we reported phantosmia as rare neurological manifestation in patient infected with COVID-19. The mechanism of phantosmia needs further study.
Background and Aims:: The competition model of the COVID19 virus and effector cells without and with vaccination is a two-cell interaction model that takes the form of a non-linear system of differential equations. The presence of vaccination may affect the behavior of the number of both cell populations. Based on the above problems, this study aims to analyze the stability of the equilibrium point of the differential equation model system and determine the dynamics of effector cells by the COVID19 virus without and with vaccination. But before that, in order to know the origin of the formation of the model, the model of the process of attacking the COVID-19 virus on the body's immunity will be analyzed.

Methods:: This study uses library research by presenting scientific reasoning arguments that describe the results of the literature review and the results of the researchers' thinking regarding the problem of the COVID19 virus model and effector cells.

Results:: The results of this study indicate that the difference in parameter values causes differences in the stability of the infection-free equilibrium point, but remains stable for the infected equilibrium point in the model without vaccination. Meanwhile, the presence of vaccination, with a fairly small value, has a significant effect on the behavior of both of them.

Conclusions:: And several types of vaccinations and changes in parameter values formed varied viral behavior, namely the logistic model and the chaotic model.
CEREBRAL VENOUS THROMBOSIS WITH NEW ONSET THROMBOCYTOPENIA AFTER ASTRazeneca’s VACCINE IN A PATIENT WITH A POSSIBLE AUTOIMMUNE DISEASE – A CASE REPORT

Miguel Miranda¹, Alexandre Fernandes², Sandra Sousa¹, Fernando Pita¹, Cátia Carmona¹, Vera Montes¹
¹Hospital de Cascais Dr. José de Almeida, Department Of Neurology, Alcabideche, Portugal, ²Hospital de Cascais Dr. José de Almeida, Physical Medicine And Rehabilitation Unit, Alcabideche, Portugal

Background and Aims:: Cases of cerebral venous sinus thrombosis (CVST) after Sars-Cov-2 vaccination, presenting with vaccine-induced immune thrombotic thrombocytopenia (VITT) have been reported in patients receiving ChAdOx1 nCoV-19 (AstraZeneca/Oxford) and Ad26.COV2.S (Janssen/Johnson&Johnson) vaccines.

Methods:: A case of a 27-year-old woman diagnosed with VITT related CVST is presented.

Results:: A 27-year-old female patient with asthma and eczema, chronically medicated with prednisolone, was admitted at the emergency department due to a left cervical and temporal pulsatile headache, worsening on Valsalva maneuver, without focal neurological deficits or papilledema. Initial laboratory work-up showed mild thrombocytopenia and a CT venography revealed a CVST of the left transverse and sigmoid sinuses and left jugular vein. The patient was started on anticoagulation and transferred to the Neurology ward for clinical vigilance, where she was further diagnosed with a pulmonary embolism. Additional work-up revealed a positive HLA-B51/B52 test and elevated C3/C4 levels, pointing to a possible autoimmune disease. Notwithstanding, further anamnesis revealed a first inoculation with ChAdOx1 nCoV-19 vaccine 10 days before headache onset, suggesting a VITT related CVST, later confirmed by a positive ELISA test for detection of PF4/heparin antibodies.

Conclusions:: In the era of vaccination against COVID-19, the presence of classical risk factors for CVST should not rule out an eventual diagnosis of VITT-related CVST. Correct and early identification of this clinical entity is vital for guiding therapeutic approaches, with direct implications over choice of acute and chronic anticoagulant drugs (non-heparin drugs preferably) and thrombocytopenia management (with immunoglobulin if persistent and severe).
NEUROLOGICAL MANIFESTATIONS OF COVID-19; A NARRATIVE REVIEW

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Background and Aims:: Many studies done during this pandemic revealed several neurological manifestations related to coronavirus disease 2019 or COVID 19 infection. The aim of this narrative review is to discuss the neurological manifestations and complications of COVID-19 disease.

Methods:: Data were retrieved from: PubMed, Scopus, Science direct in addition to manual search using Google scholar from December 2019–May 2020. Keywords were used in the search such as COVID-19; Neurological manifestations; Cranial nerves; Motor system.

Results:: Neurological manifestations and complications are common and increase with the severity of the respiratory involvement. It ranges from 34% to reach 80% in some studies. It involves the central and peripheral nervous system leading to cranial nerves palsies and limbs paralysis.

Conclusions:: Neurological complications of COVID-19 is an important determinant for the severity and mortality of patients. The virus can lead to Headache, Convulsion, Mental and Psychic changes, Delirium and Insomnia (the most affected cranial nerve is the olfactory nerve leading to anosmia), Stroke (mainly infraction), Encephalitis, Meningitis, Guillain-Barre Syndrome, Relapse of Multiple Sclerosis and Transverse Myelitis.
IMPACT OF COVID-19 RELATED DELAYS OF BOTULINUM TOXIN INJECTIONS ON THE QUALITY OF LIFE OF PATIENTS WITH DYSTONIA OR SPASTICITY

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Background and Aims:: Botulinum toxin A (BoNT-A) is considered a safe and effective treatment for spasticity and dystonia. Individual interinjections intervals are critical for the maintenance of the effect. In Austria, BoNT outpatient clinics were shutdown from November to December 2020 during COVID-19 control measures, leading to rescheduling of BoNT-A injections. This survey aimed at investigating the influence of injection delays on symptoms, physical functioning and quality of life (QoL) of the affected patients.

Methods:: Between April and June 2021, 31 outpatients (20 females, mean age: 63.7 ± 12.2 years) treated ≥12 months at the BoNT outpatient clinic Horn (Austria) and experiencing ≥2 weeks injection delays completed a structured face-to-face questionnaire.

Results:: Indications were dystonia (35.5%), spasticity (41.9%) and hyperhidrosis (3.2%). Injections were delayed by 10 weeks (median, range: 2-15). Muscle cramps increased in 94% of patients with spasticity, muscle contractions in 91% of those with dystonia, pain in 9% and 59% for dystonia and spasticity, respectively. Overall, 79% reported functional worsening, and reduces in QoL by 61% ± 17 (mean ± SD). The impact on QoL correlated with the subjective global improvement induced by BoNT-A (Rs:0.676; p<0.001). For 76%, long-term assurance of BoNT-A therapy was very important, and 79% felt their patient rights not respected.

Conclusions:: COVID-19 related delays in BoNT-A injections illustrate the importance of this therapy for symptom relief, functional outcome and QoL in patients suffering from movement disorders. BoNT-A therapy is essential and has to be guaranteed even in circumstance such as the COVID-19 pandemic.
THE EFFECT OF VIRTUAL LEARNING ON SEIZURE CONTROL AMONG EPILEPSY PATIENTS IN SAUDI ARABIA

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Background and Aims:: The COVID-19 pandemic has resulted in multiple precautions to control the infection. One of which is transforming student’s schools into virtual classrooms. This study aimed to determine the effect of virtual learning in seizure control among epilepsy patients.

Methods:: This is an online-based cross-sectional study that performed between 17 February to 27 June 2021 among patients with epilepsy who attend virtual learning classes. We included all patients aged between 12 to 30 years and living in KSA.

Results:: A total number of 70 patients were included in the study. The participants’ gender was nearly equally distributed between the two groups with females predominant (51%). Before the pandemic of COVID-19, only seven patients reported an average number of times of seizures experienced per year, while during the pandemic of COVID-19, the number were increased to 14 patients. More than have of the patients reported an increased levels of anxiety and stress due to the pandemic (43, 61.4%), and forty patients have complained of sleep disturbances due to the pandemic of COVID-19 (57.1%).

Conclusions:: Virtual learning has increased the seizure frequency in a subset of patients with photosensitive epilepsy as they are spending more time on devices.
IMMUNIZATION RELATED FOCAL NEUROLOGICAL SYNDROME AFTER CORONAVAC VACCINATION

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Background and Aims:: We report patients with focal neurological symptoms after receiving inactivated virus vaccine, CoronaVac (Sinovac Biotech, China).

Methods:: Patients who reported acute focal neurological syndrome to the hospital post vaccination surveillance program were studied.

Results:: Among 13,194 individuals who received first doses and 4,064 second doses of the CoronaVac, 49 (0.37%) reported focal neurological symptoms. Patients were age 24-48 years and 90% were female. Unilateral sensory disturbance was the most frequent symptom (92%). 66% occurred at the same side of injection. The sensory symptoms typically started in the hand and progressed to ipsilateral arm and face and/or leg. Four patients had significant hemiparesis on physical examination. Headaches were reported in 61%. Onset of symptoms was within 24 hours after vaccination in 70% and within 7 days in all. Symptom duration most commonly was for 2-4 days and resolved within 2 weeks. Of the 49 cases, 8 presented to the emergency department and received further investigations. MRI and MRA of the brain were normal in all 8 patients. Regions of hypoperfusion and concurrent smaller regions of hyperperfusion contralateral to the symptomatic side on brain SPECT imaging were seen in all studied cases while symptomatic.

Conclusions:: We propose the term Immunization Related Focal Neurological Syndromes (IRFN) for this novel clinical entity. The transient nature of the symptoms, progressive sensory impairment involving the typical areas of migraine aura together with abnormal findings on SPECT suggest cortical spreading depression as a contributing mechanism of this syndrome. Further investigations are required to understand the pathophysiology of this condition.
CEREBRAL AMYLOID ANGIOPATHY – RELATED INFLAMMATION AFTER COVID 19 VACCINATION: CASE OR CAUSALITY?

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Background and Aims:: Cerebral amyloid angiopathy (CAA) is characterized by microangiopathy with increased susceptibility to hemorrhages. Some patients may develop an inflammatory form presenting with focal deficits, seizures and alterations of vigilance (CAA-related inflammation episodes-CAA-ri). To report on clinical and biological findings of a case of CAA-ri after Covid 19 Tozinameran vaccination.

Methods:: CSF exam and brain MRI were done.

Results:: A 77 year-old male with recent brain hemorrhage in an established probable CAA presented to ER for fever and confusional state 14 days after Tozinameran first dose vaccination. Neurological examination found the patient alert, confused, with hypertonia and action tremor but no meningeal signs. Blood investigations revealed inflammation without microbiological findings. CSF study showed increased proteins, lymphocytic pleocytosis (122 cells/\textmu L) and mirror pattern. CSF Beta42 amyloid level was reduced (158 ng/L), t-Tau level increased. ApoE haplotype resulted E3/E4. The patient had refractory convulsive status epilepticus. MRI confirmed known subacute occipital hemorrhage, multiple microbleeds and occipito-parietal and frontal white matter vasogenic oedema. After a diagnosis of probable CAA-ri, high dose steroid therapy was started followed by clinical improvement and CSF normalization. Anti SARS CoV 2 antibodies were found in serum and CSF before and after steroid therapy.

Conclusions:: Following Tozinameran vaccine, a patient with probable CAA developed a systemic inflammation with neuroimaging signs of CAA-ri and persisting positive CSF anti-spike protein antibodies. We suggest that systemic inflammation evoked by anti-COVID vaccination may have induced CAA-ri in a patient with subacute intracerebral hemorrhage. Cross-reaction of anti-spike antibodies with endothelial antigens in amyloid microangiopathy should be further studied.
NEUROLOGICAL MANIFESTATIONS IN PATIENTS WITH COVID 19 AFFECTED WITH BLACK FUNGUS "MUCORMYCOSIS" : INDIA

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Background and Aims:: TO INVESTIGATE VARIOUS NEUROLOGICAL MANIFESTATIONS IN PATIENTS WITH COVID 19 AFFECTED WITH MUCORMYCOSIS
Methods:: METHODS : We analysed details of patients with mucormycosis and covid 19, admitted in Sri Ramachandra hospital, chennai from june1, 2021 to July 10, 2021 who developed various neurological features. We collected and analysed demographic features, severity of covid, comorbidities, treatment received, neurological manifestations that were present.
Results:: RESULTS: Overall, 22 cases of mucormycosis have been reported in covid patients, of which 11 cases had various neurological manifestations. Analysis showed most commonly affected were males (7(63.6%), preexisting diabetes was present in (9(81%)) cases. Various neurological features included were intracranial bleeds (2(18.2%)), orbital involvement(5(47%)), stroke(3(27.3%)), PRES(Posterior reversible encephalopathy) (1(9.1%)), cerebritis(2(18.2%)), cavernous sinus thrombosis(2(18.2%)). Surgical debridement was done in 7 patients(63%) , 2 patients died (18.2%) and 2 patients (18.2%)
discontinued the treatment.
Conclusions: Mucormycosis have been reported more from India. Mucormycosis in COVID 19 patients associated with various neurological features, due to direct invasion and systemic inflammatory syndrome. Conclusion in our study was, majority of patients had orbital apex syndrome, followed by stroke. Patients with intracranial bleed and large vessel stroke had fatal outcome. Early surgical intervention had good outcome. Patient who had moderate to severe pneumonia received anticoagulation, in spite of it, some developed stroke and treating intracerebral bleed cases was quite challenging. Further studies with larger number of patients and with control groups should be done to understand the interplay between covid 19 and mucormycosis and resulting neurological syndromes.
WORSENING OF NEUROPSYCHIATRIC SYMPTOMS AFTER SIX MONTHS FROM THE ACUTE COVID-19 INFECTION IN 1183 SUBJECTS

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**Background and Aims:** Little is known about the longitudinal evaluation after COVID-19 infection. Here, we longitudinally evaluated a large group of recovered patients to analyze the changes of systemic and neuropsychiatric symptoms.

**Methods:** We collected self-reported symptoms (twice) from 1183 patients (79% women, the median age of 41 years [range 12-77]) with confirmed Covid-19 diagnosis (1046 (88%) domiciliary treatment, 50 (4%) intensive care and 87 (7%) infirmary treatments). We conducted a longitudinal analysis, comparing the proportion of symptoms between two interviews. The analyses were performed with in-house Python scripts.

**Results:** The median interval between diagnosis and the first interview (V1) was of 75 days [range 15-395]). The median interval between the V1 and second form filling (V2) was 101 days [range 30-261]. Only 9% reported being asymptomatic on V2. Between the V1 and V2, there was an increased proportion of self-reporting fatigue (49% to 55%), memory problems (43 to 55%), motor difficulties (10 to 33%), headache (30 to 42%), and insomnia (1 to 21%), anxiety (1 to 42%), depression (1 to 19%), cardiac problems (1 to 13%), and abnormal sexual desire (0 to 22%). Some symptoms remained stable: hyposmia (27%), dysgeusia (23%), and sleepiness (36%). There was a reduction of some symptoms, including musculoskeletal pain (7 to 1%) and shortness of breath (12 to 0%).

**Conclusions:** As expected, shortness of breath improved. However, this group of patients (mostly non-hospitalized) presented worsening neuropsychiatric symptoms. Multimodal investigation with neurophysiological tests and neuroimaging will help to clarify the neural substrates of these symptoms.
MOTOR SKILLS DYSFUNCTION AND FATIGUE PERSIST AFTER MILD INFECTION BY SARS-COV 2

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Background and Aims:: Although neuropsychiatric manifestations have been reported after COVID-19, little is known about fine motor difficulties after mild infection. We evaluate fine motor impairment, fatigue, depression, anxiety and somnolence after COVID-19.

Methods:: We applied the 9-hole peg and the "box and blocks" tests to fine motor skills; and Hanoi tower test to evaluate executive functions. Individuals answered the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Chalder fatigue questionnaire (CFQ) and Epworth sleepiness Scale (ESS). We used SPSS26 with Mann-Whitney U-test to compare variables between groups and partial correlations to correlate the continuous variables.

Results:: We evaluated 23 subjects recovered from COVID-19 (after 4 months from diagnosis) (16 women; median of 39 years)) and 35 healthy controls (23 women; median 33 years) balanced for sex (p=0.8), age (p=0.3) and education (p=0.6). COVID group presented excessive sleepiness (ESS, median 10 points (range 0-18)), and fatigue (CFQ, median 18 points (range 0-32)). Fatigue correlated with depression symptoms (r=0.5; p=0.018), with anxiety (r=0.49; p=0.021), and with sleepiness (r=0.4; p=0.06). COVID group was slower on the 9-Hole Peg Test for dominant (p=0.004) and non-dominant hands (p=0.002), and performed poorer on Box and blocks test (p=0.047). They were slower on the Hanoi Tower test with 3 pieces (p=0.04).

Conclusions:: We identified persistent neurological symptoms (mainly fatigue and somnolence) motor slowness and difficulties in patients with mild infection and without hospital treatment. Fatigue associated with other neuropsychiatric symptoms. The longitudinal evaluation and neuroimaging correlations in a larger sample may clarify the duration of deficits and the associated cerebral abnormalities.
Background and Aims:: The ongoing Covid-19 pandemic has led to a lot of deaths worldwide and has been responsible for major pulmonary as well as extra-pulmonary complications. Recently, mucormycosis has come up as an important epidemic in Covid recovered immunosuppressed patients in India. It has mainly been attributed to steroid use during Covid illness and particularly in diabetic individuals. While classical presentation includes headache, nasal crusting, orbital cellulitis and multiple cranial nerve deficits, varied unusual presentations are also witnessed. One such interesting case is discussed.

Methods:: A 51 year old diabetic male underwent treatment for Covid-19 illness. After around 20 days of discharge from hospital, he developed complaint of diplopia. Examination revealed nasal crusting, mild tenderness over left cheek with left sided lateral rectus palsy with no other cranial nerve involvement.

Results:: MRI revealed orbital soft tissue thickening, inflammation of ethmoid, maxillary and sphenoid sinuses with extension of abnormal soft tissue till left superior orbital fissure. Nasal endoscopic biopsy confirmed mucormycosis. Patient was successfully managed with liposomal amphotericin B and surgical debridement.

Conclusions:: Rhino-orbital-cerebral mucormycosis is an important recent complication of COVID-19 infection which can manifest with unusual presentations like isolated lateral rectus palsy.
POST COVID-19 RHINOCEREBRAL MUCORMYCOSIS PRESENTING WITH STROKE

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Background and Aims:: COVID-19 may present with a variety of clinical features and complications like pulmonary thromboembolism, acute myocardial infarction, arrhythmias, acute stroke and other secondary infections. Mucormycosis is a dangerous invasive fungal infection characterized by vascular invasion, thrombosis and necrosis of tissues. We report an interesting case of COVID-19 infection, who developed rhinocerebral mucormycosis during the course of illness.

Methods:: A 90 year old female got admitted for treatment of COVID-19 illness. During the course of her stay, she developed left hemiparesis with left upper motor neuron (UMN) type facial palsy. This was preceded by left sided facial pain, nasal discharge and crusting.

Results:: CT head and paranasal sinuses was done which showed right MCA territory acute infarct with few hyperdense areas in left maxillary sinus with obliteration of left maxillary ostium suggestive of fungal sinusitis. Biopsy of paranasal sinuses was done which showed broad, ribbon-like non-septate hyphae consistent with mucormycosis. Surgical debridement was done and antifungals were given.

Conclusions:: Mucormycosis is an emerging important complication of COVID-19 infection. Prompt diagnosis of this life-threatening condition is needed for early initiation of treatment for improved survival.
DIAGNOSIS OF THROMBOSIS OF CEREBRAL VESSELS AND VENOUS SINUSES IN PATIENTS WITH MAXILLOFACIAL COMPLICATIONS AFTER COVID-19

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Background and Aims:: It is known that with Covid-19, blood clotting increases, the coagulopathy is the cause of thrombosis of the vessels, also of the brain, face. Diagnostics of thrombosis of cerebral vessels and venous sinuses in patients with maxillofacial complications after Covid-19

Methods:: In the multidisciplinary clinic of the Tashkent Medical Academy, 78 patients were diagnosed with thrombosis of the cavernous sinus, osteomyelitis of the upper jaw. The average age of patients was 60 ± 8 years, of which 41 were women (51.3%) and 37 were men (48.7%). All patients underwent MSCT / MRI of the brain with angiography

Results:: MRI imaging aids in the identification of thrombosis, either through direct visualization of a thrombus/filling defect in the cavernous sinus, or through indirect signs including proptosis, dilation of drainage tributaries, and abnormal strengthening of the dura, which well demonstrated in contrast-enhanced studies. According to analysis, thrombosis of A. oftalmica in 60% (p≤0,05)(Fig. 1.2)
thrombosis of the cavernous sinus 22% (Fig. 3), thrombosis of the A. Maxillaris
A. Sphenopalatina) 7%, narrowing of the internal
Carotid artery 24% of cases ... In addition, orbital lesion, which is indicated by abnormal orbital fat density by signal intensity, is well indicated along with other features such as narrowing of carotid artery, intraparenchymal abnormalities such as cerebral infarction, empyema, meningitis, cerebritis, and abscess.

Conclusions: CT / MRI shows the presence of heterogeneous and asymmetric defects, tributary thrombosis, dura mater sinuses, and cerebral veins, which is important to this condition, deciding on the need for anticoagulation and surgical treatment.
Guillain Barre Syndrome and Subsegmentary Pulmonary Embolism Associated to SARS COV 2 Infection. Case Report and Review of Current Literature.

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Background and Aims:: There’s emerging evidence on the association of GBS with SARS-CoV-2 infection. Neurotropism by coronavirus has been documented as well as various neurological manifestations such as encephalitis, stroke, encephalopathy and peripheral nerve disease.

Methods:: A 67-year-old male, no comorbidities presents three weeks prior to admission with fever, cough, taste and smell disturbances, myalgias, asthenia, clumsy hand movements and progressive lower limbs weakness. 15 days prior to admission: difficulty swallowing, diaphoresis. At admission: breathing difficulty and palpitations. Glasgow 13 E4 V5 M4, bulbar compromise, bradylalia, diminished gag reflex, sternocleidomastoid and trapezius weakness, MRC scale upper and lower limbs: proximal 3/5 distal 2/5, generalized areflexia, distal diffuse hypoesthesia

Results:: Ferritin 519 LDH 236 D Dimer >10,000 Hgb 19 WBC 11590 L 12% N 80% P 241,000 CK 111 CK MB 17. Chest CT: COVID19 pneumonia, CO-RADS 3. Pulmonary angiography: Posterior right lower lobe segmental PE. Scores: PESI 108, Geneva 10. SARS-COV-2 PCR negative, SARS-COV-2 IgG/IgM: Positive. Lumbar puncture not performed due to PE. Met Asbury GBS criteria, HUGHES 4, mEGOS 8 at admission, EGRIS 4. Progression of ascending symmetrical bilateral flaccidity with respiratory failure requiring mechanical ventilation for 10 days, tracheostomy and gastrostomy were performed. Discharged at day 60 with muscle strength recovery, upper limbs 4/5 and lower limbs 3/5, Sensitivity recovery, diminished lower limb reflexes. Therapy: Enoxaparin 60mg every 12h, Immunoglobulin 0.4mg/kg/day/5 doses. Discharge HUGHES 3.
Conclusions: GBS is caused by an anomalous response of the immune system to an infectious agent. This particular patient presents with a GBS associated with SARS-COV-2 infection and PE.
EFFECT OF INACTIVATION MODE ON SECOND-GENERATION ANTIPSYCHOTIC TDM UNDER COVID-19

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Background and Aims:: To study the effect of heating at 56 °C for 30 min on the monitoring of five second-generation antipsychotics (aripiprazole, quetiapine, risperidone, clozapine and olanzapine).
Methods:: After the plasma samples were treated with protein precipitation, the concentrations of aripiprazole, quetiapine, risperidone, clozapine and olanzapine were determined by LC-MS method before and after inactivation of plasma quality control substances and clinical samples. Bland-Ahman method was used to evaluate the difference between the inactivated and non-inactivated determination results, and the correlation between the determination results was analyzed by Passing-Bablok regression and linear regression.
Results:: The five second-generation antipsychotics could remain stable after inactivation, and there was no significant difference in matrix effect before and after inactivation of serum quality control substances, and the concentration percentages before and after inactivation were all within the normal range.
Conclusions:: the combination of 56 °C for 30 min inactivated protein precipitation treatment method of plasma samples of LC - MS determination made pp, quetiapine, risperidone, clozapine, olanzapine plasma concentration is affected, the determination results have good consistency and relevance, o can be used to make pp, quetiapine, risperidone, clozapine, olanzapine routine therapeutic drug monitoring.
LOW STROKE ADMISSIONS AND MORTALITY DURING COVID-19 LOCKDOWN; LINK TO AIR QUALITY INDEX

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Background and Aims:: Air pollution is one of the leading causes of mortality and morbidity. It accounts for 21% of stroke-related deaths and about 170 million disability-adjusted life years. Both long-term and short-term exposures to air pollution are markedly associated with ill health effects. COVID-19 pandemic and the subsequent global lockdown have led to a reduction in air pollution levels.

Methods:: All admitted stroke patients during the five months of lockdown from March to July 2020 are included and compared to the number of stroke admissions during the same five months in the previous two years, i.e. 2019 and 2018. The patients were further stratified into gender, stroke type, and mortality rates. Available online air quality index (AQI) of Karachi, Pakistan was also accessed.

Results:: 182 stroke patients were admitted compared to the 355 and 299 stroke patients admitted during the same months in 2019 and 2018, respectively. No gender or stroke type differences were noticed. However, a disparity was seen in the mortality rates (2.74% in 2020 vs 8.16% in 2019 and 12.04% in 2018). The average AQI of Karachi in the last nine days of May 2019 was 1.6 times higher than the same period in 2020 (102.11 vs 64.33). Similarly, average AQI was higher in 2019 compared to 2020 during the months of June (87.13 vs 73.03) and July (89.64 vs 65.09).

Conclusions:: Approximately 50% reduction in stroke cases is noticed during the lockdown. One of the suggested contributing factors is a reduction in air pollution, although further studies are needed to confirm.
PARANEOPLASTIC NEUROLOGICAL SYNDROME ASSOCIATED WITH ANTI-AMPHIPHYSIN ANTIBODIES MISLEADE THE DIAGNOSIS OF CREUTZFELDT-JAKOB DISEASE

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Background and Aims:: Creutzfeldt-Jakob disease (CJD) and neurological paraneoplastic disease may present similar clinical features. Establishing the correct diagnosis has practical relevance in the care management for these patients. The objective of the present study is to determine how the diagnosis of Creutzfeldt-Jakob disease may be differentiated from several rapidly progressive neurological syndromes.

Methods:: Here we describe a case of Creutzfeldt-Jakob disease associated with anti-amphiphysin antibodies. In July 2016 a 66-years old female patient was admitted to our acute neurological department with progressive walking disturbances for two months. Neurological examination showed cerebellar syndrome characterized by gait, truncal and limbs ataxia, tremor towards the end of upper limbs movements, absent deep tendon reflexes, bilateral nystagmus with impaired up- and lateral gaze.

Results:: Biochemical and serological investigations were unremarkable except of the presence of anti-amphiphysin autoantibodies both in serum and cerebrospinal fluid (CSF) (Yo, HU, Ri, PNMa2, CRMP5 autoantibodies were negative). Brain MRI (Fig. 1) and electroencephalogram (Fig. 2) reported findings suggestive for CJD. Cerebrospinal fluid was unremarkable but protein 14.3.3, tau-protein (> 2350 pg/ml) and RT-QuIC test were positive. Prion protein gene studying revealed heterozygosity Met/Val polymorphism at codon 129. After plasmapheresis, despite the removal of anti-amphiphysin autoantibodies the patients progressed to deteriorate and she died 5 months after symptoms onset. Brain autopsy confirmed sporadic sCJD.
Conclusions:: To our best knowledge, this is the first report about the association of anti-amphiphysin antibodies and CJD and the coincident of onconeural autoantibodies seems not to correlate with sCJD pathogenesis.
ACUTE ONSET GENERALIZED WEAKNESS: A RARE VARIANT OF MULTIFOCAL MOTOR NEUROPATHY

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Background and Aims:: Multifocal motor neuropathy (MMN) is a slowly progressive asymmetrical focal demyelinating neuropathy. We present a patient consistent with acute multifocal motor neuropathy with conduction blocks (AMMNCB).

Methods:: A 69 year old woman presented with acute onset generalized weakness in 2009, 2013, 2016 and responded to intravenous immunoglobulins (IVlg). In 2020, she presented with acute onset bilateral lower limb weakness, evolved very rapidly causing generalized weakness within a day. She had asymmetrical lower limb weakness and symmetrical upper limbs involvement with global areflexia. Cranial nerves, sensory, autonomic or sphincter involvement was not present.

Results:: Nerve conduction study (NCS) disclosed wide spread motor CBs in non-compressive sites with diffuse F wave abnormalities with normal sensory conduction. Serology revealed positive anti-GM1 antibodies without cyto-protein dissociation in csf done after 2 weeks. She responded to IVlg. Follow up NCS after a month revealed persistent motor CBs despite clinical improvement.

Conclusions:: Acute motor axonal neuropathy (AMAN), acute inflammatory demyelinating polyradiculopathy (AIDP) and chronic inflammatory demyelinating polyradiculopathy (CIDP) were considered in this clinical context. Definite CB is not usually seen in AMAN apart from rare form, AMAN with reversible conduction block variant. AIDP shows definite CBs which disappear with IVlg and also upper limb sensory involvement with sural sparing is classical. Sensory sparing and motor CBs observed alone without any other features of demyelination are against the diagnosis of CIDP. Therefore, the presentation with acute onset generalized weakness with above described electrophysiological evidence and serological confirmation are consistent with AMMNCB, a rare presentation of MMN.
PROGRESSIVE MYELOPATHY DUE TO TREATABLE INTRACRANIAL DURAL ARTEROVENOUS FISTULAE

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Background and Aims:: Intracranial dural arteriovenous fistulae (DAVF) can rarely have a perimedullary venous drainage (Cognard Type V) resulting in an aggressive but potentially treatable and reversible myelopathy. Early diagnosis is often challenging.

Methods:: A 52 years-old man has come to our attention 8 months after the onset of a stepwise progressing myelopathy. Neurological examination showed quadriaparesis, ankle clonus, urinary retention and bowel incontinence along with abolished pain, temperature and statokinesthetic sensations below D10.

Results::

Spinal MRI showed cervical spinal cord swelling with T2-weighted sequences hyperintensity (previously interpreted as expression of myelitis - the patient was started on steroids without significant improvement) and tortuous flow-voids behind the spinal cord, expression of congested medullary veins. Brain MRI
demonstrated T2/FLAIR hyperintense lesions in the pons and in the right cerebellar hemisphere with focal hemosiderin deposits along the inferior cerebellar sulci. CSF analysis (with isoelectrofocusing), serum autoantibodies, a total body CT were negative. Brain angiography revealed a DAVF of the inferior wall of the straight sinus draining into the perimedullary venous plexus. Despite the successful endovascular treatment, the patient showed a mild improvement of the strength in his upper limbs but after 6 months he was still confined to the wheelchair.

**Conclusions:** DAVF are often under-recognized and misdiagnosed as infective myelitis, transverse myelitis, Multiple Sclerosis, Neuromyelitis Optica Spectrum Disorder or neoplasms. We thus suggest performing an angiography of cerebral vessels in the few cases of progressive myelopathy in which routine tests for myelitis are inconclusive, closely looking for perimedullary flow voids and/or serpiginous vessels on spinal cord MRI.
HYPNOSIS AND VIRTUAL REALITY IN PSYCHOTHERAPY

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Background and Aims:: Hypnosis and virtual reality are already used separately in psychotherapy, but the associated effect of both techniques increases the influence of each, as virtual reality favours the narrowing of the field of consciousness induced by hypnosis, amplifying its effects: it is an all-encompassing experience that all users report as very engaging. It has been observed that the trance sometimes develops even without induction.

Methods:: The work is conducted through the use of a visor and the induction of the trance after the start of various videos, of varying duration. At the setting of hypnosis (armchair, adequate environmental temperature, attenuation of external stimuli) we add the use of the viewer in which first abstract videos such as geometric representations, lights and colors are transmitted to hinder the projections of the subject, and then concrete videos, depicting naturalistic scenarios associated with brief stimulus stories, used as a metaphor to guide the subject towards more appropriate behavioural styles. The therapist observes simultaneously on another screen what is transmitted by the viewer, so as to gradually follow the subject and accompany him with suggestions. The state of trance is maintained and it is not interrupted by the visual and auditory stimuli to which he is subjected.

Results:: At the moment everyone has experienced a drop in anxiety and reinforcement of the ego.

Conclusions:: The work started a few years ago, but the relative effects are encouraging, with the participants who do not develop any idiosyncrasies, but instead they are very satisfied with the experience and motivated.
COVID-19 PANDEMIC IN LOMBARDY: RISK PERCEPTION AND COPING STRATEGIES OF AGING PEOPLE

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Background and Aims:: During the COVID-19 pandemic, older adults are the segment of the population at higher risk for health and isolation. Exploring aging people needs and reactions to the situation it’s crucial to plan appropriate interventions and supporting strategies. The present study aimed to investigate risk perception and coping strategies in older adults during the COVID-19 pandemic in Italy.

Methods:: 514 people over 65 years, residing in the Lombardy region of Italy, were administered with a structured online interview collecting socio-demographic information, sources of information used, daily actions undertaken to avoid the contagion, risk perception related to COVID-19 and other threats, and coping strategies used to face the situation.

Results:: Risk perception related to COVID-19 was significantly lower than the perceived risk associated with other threats, and it was correlated to the number of sources of information used. Most of the sample relied on avoidant coping strategies with a tendency to accept the situation by avoiding stressors more than rebelling to the situation with approaching strategies.

Conclusions:: Participants put into action most of the possible behaviors aimed to avoid contracting the COVID-19, showing a tendency in using avoidance strategies. This confirmed that the choice of the best strategy to use depends on the features of the situation a person must face. Regarding risk perception, it is necessary to take into consideration its link with the perception of control: the lockdown condition lets older adults to feel safer and less vulnerable to the virus.
PROGNOSIS OF EARLY ONSET OF ALZHEIMER’S DISEASE UP 6 YEARS IN ADVANCE BY A CONFORMATIONAL VARIANT OF P53 (U-P53AZ)

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Background and Aims:: Recently, a conformational variant of p53 (U-p53AZ) has been identified as a lead biomarker for Alzheimer’s Disease (AD). A highly sensitive, specific and reliable IP-SACI-MS (described as AlzoSure® Predict) was used to detect U-p53AZ in plasma samples from AD-individuals at different stages of the disease to validate its AD-dementia prognostic value.

Methods:: 262 plasma samples from 225 participants (70y average in age) at different cognitive stages from Australian Imaging, Biomarkers, and Lifestyle (AIBL) retrospective longitudinal cohort were selected. Clinical groups included Cognitively Normal (CN; n=75) and Mild Cognitive Impairment (MCI; n=30) participants not progressed to AD or dementia over 6 years, CN (n=42) and MCI (n=49) who progressed to AD at different follow-up time points over 6 years, and AD (n=18) and other disorders (OD, n=10). AZ 284™ peptide, from U-p53AZ was quantified by IP-SACI-MS method (AlzoSure® Predict).

Results:: Preliminary cutoff of AZ 284™ to predict AD-dementia, were calculated using optimal Youden Index, 95% CI. U-p53AZ prognostic performance to AD-dementia (CDR>0.5) was evaluated by AUC, PPV, NPV and they were >90% for both Subjective Memory Compliants (SMC) (CDR=0) and MCI-non demented (CDR=0.5) progressed to AD (CDR>0.5) in a follow-up period from 1.5y to >6y. U-p53AZ showed an high AUC value =95% to diagnose individuals CDR ≥1, PiB-PetPOS and diagnosed as AD. By a regression model combining U-p53AZ with PiB-Pet data, age/ gender, APOE4 it was demonstrated the covariates didn’t significantly improve U-p53AZ AD-prognostic value.

Conclusions:: This study the U-p53AZ AD-Dementia prognostic value and its utility in the pathway of AD prognosis.
EVALUATION OF BLOOD PRESSURE VALUES IN PATIENTS WITH TRANSIENT GLOBAL AMNESIA: A SINGLE CENTER EXPERIENCE.

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Background and Aims:: Transient Global Amnesia (TGA) is a syndrome characterized by a sudden anterograde and often a retrograde amnesia lasting less than 24 hours, in absence of other neurological focal signs. Its pathophysiologic mechanism is still unclear, but different hypotheses and trigger factors have been proposed. This study aimed to assess blood pressure values in patients diagnosed with the TGA at admission and at 24 hours after the onset of symptoms and to identify the degree of hypertension during and after the TGA attack.

Methods:: We retrospectively examined data of patients affected by TGA, who were admitted to our center from December 2012 to December 2020. The clinical diagnosis has been based on Hodges and Caplan criteria. BP values have been classified according to 2020 International Society of Hypertension classification.

Results:: We included 54 patients, 24 males (44%) and 30 females (56%). The mean age at the TGA attack was 62.7 years. 31 patients had a history of hypertension and 27 were in pharmacological treatment. Valsalva or Valsalva-like maneuvers were associated with the onset of TGA symptoms only in 3 patients. At admission 18.5% had normal BP values; 1.8% had high normal BP; 29.7% had grade 1 hypertension and 50% had grade 2 hypertension. At 24 hours from the onset of AGT 51.2% had a normal BP; 27.9% had high normal BP; 20.9% had grade 1 hypertension and no one had grade 2 hypertension.
Conclusions:: Our study suggests hypertension as possible TGA trigger factor, but we need more patients to determine its causative role.
THE TREND OF INCIDENCE AND BURDEN OF NEUROLOGICAL DISEASE IN IRAN BETWEEN 1990 AND 2017: BASED ON THE GLOBAL BURDEN OF DISEASE ESTIMATIONS

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Background and Aims:: Neurological disease contributes significantly to morbidity and mortality in different ages and geographic areas around the world. The purpose of the current study was to investigate the incidence and disability-adjusted life years (DALYs) trend of neurological disease in Iran 27 years ago.

Methods:: We used the data of the Global Burden of Disease (GBD) Study to estimate the incidence and DALYs of neurological disease in Iran in different age groups between 1990 and 2017. Age groups were defined into 5 groups including < 5 years, 5-14 years, 15-49 years, 50-69 years, and ≥ 70 years.

Results:: The incidence number of neurological diseases from 1990 to 2017 increased from 7.5 million to more than 12 million and the incidence rate grew as much as 1400 per 100000 populations in Iran. Totally, headache, epilepsy, and Alzheimer's disease were the most common neurological diseases according to incidence and had the most values of DALY in Iran. The highest incidence and DALY of neurological disease was observed in the age group of 15-49 years.

Conclusions:: This study showed that the incidence and burden of neurological diseases had a dramatic increasing trend 27 years ago in Iran. Consequently, it is necessary to investigate the causes of the growing trend in future studies.
Background and Aims:: SSPE is chronic progressive encephalitis affecting children and young adults which usually presents with cognitive decline and behavioural changes followed by periodic myoclonic jerks, seizures, vision loss and ataxia. High degree of suspicion is required as the presentation can be variable and can have many differentials. We aim to study various presentations of SSPE.

Methods:: Retrospective study was done to analyse various presentations in patients diagnosed with SSPE as per modified Dykens criteria from a tertiary care centre over a period of 2 years (1st January 2018-31st December 2020).

Results::

![EEG showing slow sharp wave generalised quasiperiodic discharges](image-url)
6 cases of SSPE were identified. Case 1 - 22 months old presented with subacute history of ataxia, multifocal myoclonus and developmental regression. Gradually myoclonus worsened to involve trunk and developed drop attacks. Case 2 - 17 years boy presented with single episode of seizure. Case 3 - 25 years female with 5 months gestation presented with sub acute vision loss followed by progressive cognitive decline, behavioural changes, Parkinsonism, Dystonia and stimulus sensitive myoclonus. Case 4 - 28 years female presented with rapidly progressive cognitive decline and behavioural changes. Case 5 - 32 years male presented with history of myoclonic jerks and dropping of objects. Gradually developed progressive behavioural changes and cognitive decline and became vegetative. Case 6 - 9 year old child presented with faciobrachial seizures (myoclonic jerks) and scholastic backwardness.

**Conclusions::** SSPE can manifest with varied presenting complaints. Also, Results of EEG, MRI and CSF examination can change during the disease course. Therefore, high degree of suspicion is required for early diagnosis of this challenging entity.
HUFFER’S NEUROPATHY: A CASE OF ACUTE-ONSET TETRAPARESIS MIMICKING GUILLAIN-BARRÉ SYNDROME.

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Background and Aims:: N-hexane is a well-known neurotoxic agent causing chronic peripheral neuropathy with predominant motor involvement. Originally described as a result of occupational exposure in various industrial settings, only few reports exist on polyneuropathy due to recreational inhalation of glues and solvents.

Methods:: We herein report an unusual case of a 40-year-old woman presenting to the emergency department with acute-onset tetraparesis due to inhalation of chemical solvents containing n-hexane. The clinical picture, a mild albumin-cytologic dissociation and the demyelinating features on nerve conduction study initially mimicked the presentation of Guillain-Barré syndrome (GBS), but the patient failed to respond to intravenous immunoglobulin treatment and plasma exchange. Diagnosis of hexane-induced neuropathy was then confirmed by means of sural nerve biopsy, showing axonal enlargement with secondary retraction and thinning of the myelin sheath (Figure 1 and 2).
**Results:** We highlight the challenges faced in the differential diagnosis of acute-onset polyneuropathy as well as the electrodiagnostic and neuropathologic features of hexane neuropathy.

**Conclusions:** N-hexane polyneuropathy should be considered a possible differential diagnosis of GBS in patients with poor response to appropriate treatment and a history of substance abuse.
QUALITY CONTROL IN BIOBANK SAMPLES: THE IMPACT OF PRE-FREEZING STORAGE TIME AND TEMPERATURE ON GENE EXPRESSION OF BLOOD COLLECTED IN EDTA TUBES

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Background and Aims:: Blood gene expression profiling is taking hold in research, diagnosis and monitoring of human diseases. Blood is vulnerable to pre-analytical variables that may alter gene expression ex vivo. Although RNA stabilization systems have been shown to reduce such influence, traditional EDTA tubes are still widely used since they are less expensive and enable to study specific leukocyte populations. Nevertheless, studies on the impact of short bench times on gene expression are lacking.

Methods:: Nine EDTA tubes were collected from 10 healthy donors. One tube from each donor was immediately processed for mononuclear cell isolation, while the others were kept at either 4°C or room temperature for 2, 4, 6 and 24 hours. RNA yield and quality and the expression level of 4 housekeeping (B2M, CASC3, GAPDH, HPRT1) and 8 target genes (CD14, CD19, CD20, IL10, MxA, TNF, TNFAIP3, NR4A2) were evaluated.

Results:: RNA yield, quality and integrity did not vary significantly with time and temperature. B2M was the most stable housekeeping gene, while the others were increasingly influenced by storing time, especially at 4°C. Even when normalized to B2M, the expression level of some target genes, particularly TNFAIP3 and NR4A2, was highly affected by delays in blood processing at either temperature, already from 2 hours.

Conclusions:: Pre-analytical processing has a great impact on transcript expression from blood collected in EDTA tubes, especially on genes related to inflammation. Storage at low temperature does not prevent gene expression alteration. Standardized procedure of blood collection and manipulation are needed to obtain reliable results.
EAN GUIDANCE FOR DEVELOPING AND REPORTING CLINICAL PRACTICE GUIDELINES ON RARE NEUROLOGICAL DISEASES

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Background and Aims:: Rare diseases affect up to 29-million people in the EU, and almost 50% of them affect the nervous system or muscles. Delays in diagnosis and treatment onset, and insufficient treatment choices are common. Clinical Practice Guidelines (CPGs) may improve the diagnosis and treatment of patients and optimize care pathways, delivering the best scientific evidence to all clinicians treating these patients. We set recommendations for developing and reporting high-quality CPGs on rare neurological diseases (RNDs) within the European Academy of Neurology, through a consensus procedure.

Methods:: A group of 27 experts generated 93 initial items that were evaluated through a two-step
Delphi-consensus procedure and a face-to-face meeting. The final list of items was reviewed by an external-review group of 58 members.

**Results:** The consensus procedure yielded 63 final items. Items are listed according to the domains of the AGREE instruments and concern scope and purpose, stakeholder involvement, rigour of development, and applicability. Additional items regard reporting and ethical issues. Recommendations are supported by practical examples derived from published guidelines and are presented in two tables: 1. items specific to RND-CPGs, and general guideline items of special importance for RNDs, or often neglected; 2. items for guideline development within the EAN.

**Conclusions:** This guidance aims to provide solutions to the issues specific to RNDs. We consider this consensus document, produced by many experts in various fields, to serve as a starting point for further harmonization and increasing the quality of CPGs in the field of RNDs.
CARPAL TUNNEL SYNDROME IN CLEANERS AT GENERAL HOSPITAL FOR STATE SPECIAL SERVANTS

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Background and Aims:: Carpal tunnel syndrome (CTS) is caused by pressure on the median nerve. When the median nerve is compressed, the symptoms can include numbness, tingling and weakness in the hand and arm. The anatomy of your wrist, health problems and possibly repetitive hand motions can contribute to CTS. Anamnesis and clinical examination are important for diagnosis, but electrophysiological tests play a key role in confirming the diagnosis and determining the severity of the neurological damage. The reason for conducting this study is that there is no study in our country that confirms CTS by electrophysiological analysis and identifies severe and mild disorders. We aimed to diagnose CTS among hospital cleaners through anamnesis, clinical and electrophysiological tests, identify risk factors, and determine the degree of nerve damage based on clinical criteria and electrophysiological tests.

Methods:: All female floor cleaners of General Hospital for State Special Servants were enrolled. Clinical and electrophysiological severity of CTS were evaluated with standardized scales and symptoms were assessed with self-administered Boston Questionnaire; risk factors and durations of current and previous rise occupations were recorded. Univariate analysis of risk factors was performed in workers with and without CTS.

Results:: Out of a total of 28 cleaners, mean age 39.2 years (23-56 years) were enrolled in the study; 9(32.14%) had CTS (diagnosis based on clinical and electrophysiological findings). Univariate analysis showed that cleaners with CTS were older and higher BMI of high risk of developing carpal tunnel syndrome than those without CTS.

Conclusions:: These results indicate a high occurrence of CTS in cleaners.
CLINICAL CASE STUDY: PIECING THE PUZZLE OF A PRESSURE ULCER.

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**Background and Aims:** Patient male, 49 years, presented to the Emergency Department (ED) with fever and lethargy (3/7) on a background history of Spina bifida with myelomeningocele and paraplegia. On examination of the patient, a severe sacral pressure ulcer was noted. As noted by Moore et.al., pressure ulcers are common. The mean prevalence is estimated at 16% in acute and long stay settings in Ireland (Moore, Johanssen, & van Etten, 2013). Pressure ulcers are a particular complication for patients with myelomeningocele (Plaum, Riemer, & Frøslie, 2006).

**Methods:** After examination of the patient, a number of differential diagnosis were noted including trauma, osteomyelitis, moisture associated dermatitis and unstageable pressure ulcer. The patient was diagnosed with a grade 4 pressure ulcer.

**Results:** The orthopaedics and plastics MDTs assessed the patient and debridement of the wound was done by the orthopaedic team and grafting of the wound by plastics. The infectious disease team advised that the patient be put on, long-term antibiotics.

**Conclusions:** With the combined efforts of the MDT in Ballinasloe hospital, the MDT in GUH and the community MDT, this patient had a medically successful outcome and was discharged home.
NAPROXEN-INDUCED ASEPTIC MENINGITIS

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Background and Aims:: Drug-induced aseptic meningitis is an uncommon side effect of certain widely prescribed drugs. Several non-steroidal anti-inflammatory drugs (NSAIDs) have been linked to aseptic meningitis, especially in patients with immune dysfunction. Drug-induced aseptic meningitis is difficult to diagnose, and infectious causes must be ruled out. NSAIDs should be considered in the differential diagnosis in evaluating meningitis of unclear etiology.

Methods:: Case Report

Results:: A 33-year-old young woman with a history of mixed connective tissue disease had been suffering from headaches for the past five days and had developed altered sensorium one day before admission. She had been self-medicating for arthralgia with naproxen (250 mg/day) for 6 months and had recently increased the dose to 500 mg/day 4 days prior to admission. She was restless and irritable in the emergency room. Her vital signs were within normal limits. Neurological examination revealed severe neck stiffness. CSF analysis showed lymphocytic pleocytosis, low sugar and elevated protein levels. An empirical treatment of ceftriaxone and vancomycin was initiated. CSF viral, bacterial and fungal studies yielded negative results. MRI brain was unremarkable. Based on her CSF profile, her history of mixed connective tissue disease and the temporal relationship between naproxen use and symptom onset, her symptoms were thought to be due to Naproxen-induced aseptic meningitis. The antibiotics were stopped after 3 days. She was discharged on her seventh day of admission without any neurological sequelae.

Conclusions:: The clinician should keep the diagnosis of drug induced aseptic meningitis in the differential diagnosis, when there is a temporal association with a culprit drug.
IS THERE AN IMPORTANT EFFECT OF THE TYPE OF POLYNEUROPATHY ON RESULTS OF ELECTROMYOGRAPHY AND PAIN

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Background and Aims:: The patients with polyneuropathy (PNP) have serious complaints such as sensory, motor, and pain problems. The type of PNP may also be an important factor on these symptoms in patients with PNP. The aim of this study was to research the presence of difference in terms of sensory, motor and pain outcomes in patients suffered from PNP dependent to diabet, chemotherapy or other causation.

Methods:: Thirty-six patients suffered from PNP (12 female, 24 male; 12 PNP dependent to PNP, 10 PNP dependent to chemotherapy, 14 PNP dependent to other reason) were included in our study. Participants' nerve conduction characteristic including amplitude and velocity and pain assessment including pain levels and severity of neuropathic pain were assessed by Electromyography, Visual Analogue Scale (VAS), Leeds Assessment of Neuropathic Symptoms and Sign (LANSS), respectively.

Results:: The mean age of participants was 58.33 ± 15.29 years. When the groups were compared in terms of electromyography and pain evaluation results, It was seen that the groups had similar properties in terms of nerve conduction amplitude, rate, pain level and severity (p>0.05).

Conclusions:: It was determined that the type of PNP has no important effect on nerve conduction and pain properties in patients with PNP. The current findings indicate that similar treatment may be applied in managing these symptoms in all type of PNP.
Background and Aims:: Dural arteriovenous malformation (AVM) is rare but is the commonest vascular malformation encountered in the spinal cord. They cause progressive tetraplegia or paraplegia and significant morbidity. Spinal AVMs are treatable. We present a case of an acute cord compression in a young teenage girl due to a spinal AVM.

Methods:: An 18 year old girl presented with acute onset right lower limb weakness and left lower limb numbness with urine retention. Examination revealed wasted but spastic right lower limb with absent proprioception. Muscle power was MRS grade 0 on the right side and MRS grade 4 on the left. She had a sensory level at T2 on the left for pain and temperature, a band of pain and temperature loss in right side from T2 to T10. Plantar was extensor in right side, equivocal in left side. Other systemic examinations were normal.

Results:: Her MRI pan spine showed a dural arteriovenous malformation (AVM) extending from T6 to T10 with cord oedema up to T1 level bilaterally. Her MRI brain did not show any vascular anomalies. Her haematological evaluation was normal. She was treated with intravenous steroids and was subjected to a digital subtraction angiogram (DSA). The DSA confirmed the AV malformation with a feeding artery arising at T11. She underwent endovascular coil embolization and made a remarkable recovery following the intervention.

Conclusions:: Dural AV malformation is a rare but a treatable cause of progressive tetraplegia or paraplegia even in the young. Clinical presentations can be varied. Early diagnosis and appropriate intervention significantly reduces morbidity.
Background and Aims:: Globally heat stress is the silent health peril which gain attention when the body means of handling its thermoregulatory function starts to fail. The present study has been designed to investigate the nephroprotective potential Green Tea Extract (GTE) & Hesperetin in Heat Stress Induced Nephropathy (HSN).

Methods:: There were five groups in the present study and each group was comprised of six animals. Lacca mice was exposed to heat (39.5 degree C for 30 min, 2 time’s day) with DNP for 10 days. After 30 minutes’ exposure to heat mice were returned to their cages. This cycle was repeated twice a day for 10 days except the weekend. Renal histology, Biochemical parameters (BUN & sCr) & Oxidative parameters (TBARS, SOD, GSH) were performed. The experimental protocol reg. No. is USPS/IAEC/CPCSEA/2020/Protocol No. 49.

Results:: Pretreatment with GTE & Hesperetin (50mg/kg) for 10 days' results nephroprotection. It was noted that GTE and Hesperetin significantly restored the oxidative stress which was assessed by TBARS, SOD and GSH. Moreover the nephronal damage was assessed by histopathological examinations. However, the combination of GTE and Hesperetin showed the synergetic nephroprotection by decreasing oxidative stress followed by upregulation of eNOS in HSN.

Conclusions:: The nephroprotective potential of GTE & Hesperetin may be due to upregulation of eNOS followed by downregulation of ROS. The combination of GTE & Hesperetin showed additive effect which may be good potentiate for pre-clinically as well as clinically upcoming research specially targeting on Vascular endothelial dysfunctioning.
POSSIBLE POTENTIAL OF GLIMEPIRIDE WITH ORAL AMINO ACIDS IN TYPE 2 DIABETIC RATS

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Background and Aims:: Diabetes Mellitus (DM) is a major threat to global public health since the number of diabetic patients is rapidly increasing worldwide. According to International Diabetes Federation, DM will affects about 592 million by 2035. The present study has been designed to investigate the possible potential of Glimepiride with oral amino acids in type 2 DM

Methods:: Six groups were employed and each group comprised six Rats. DM induced by high fat diet (HFD) followed low dose of Streptozotocin (STZ) (35mg/kg i.p). Type 2 DM was assessed by measuring the blood glucose level. Moreover, the body weight, triglycerides, total cholesterol, high density lipoprotein, very low density lipoprotein and oxidative stress were also measured.

Results:: HFD-STZ showed significantly increased in blood glucose, body weight, triglycerides, total cholesterol, low density lipoprotein, very low density lipoprotein and oxidative stress in the present study. Moreover, HFD-STZ treated rats significantly decreased the high density lipoprotein and antioxidant enzyme. Treatment with Glimepiride (1mg/kg and 2 mg/kg, i.p.) and amino acids (250mg/kg, p.o) for 21 days produced the antidiabetic potentials dose dependently in diabetic rats. Moreover, treatment significantly increased the reduced form of glutathione, superoxide dismutase and high density lipoprotein level dose dependently.

Conclusions:: The oral amino acids in combination with Glimepiride showed synergistic antidiabetic may be due to increase the activity of insulin receptor tyrosine kinase and reducing the conductance of ATP sensitive K+ channels by acting on pancreatic β cell membrane may be a novel therapeutic approach for the management of type 2 DM.
Background and Aims:: Sensory ganglionopathy (SNN), is a disease of dorsal root ganglia and usually associated with paraneoplastic syndromes (anti-Hu associated), Sjögren syndrome, chemotherapeutic agents and paraproteinemia. Spinal MRI shows dorsal column involvement mimicking subacute combined degeneration of the cord. We present 3 cases of confirmed SNN with characteristic MRI findings.

Methods:: Case 1: A 17-year-old girl presented with difficulty in walking, recurrent falls, hand and right-facial numbness for 2 months. Case 2: A 50-year-old male presented with lower limb weakness, numbness and fecal incontinence for 4 years duration. Case 3: A 43-year-old female presented with recurrent falls and lower limb numbness for 1 year. All had areflexia with flaccid paralysis and impaired proprioception, vibration with a positive Romberg’s test. NCS were suggestive of sensory ganglionopathy and MRI spine (Figure 1) revealed dorsal column hyperintensity without contrast enhancement. Serum B12 level was 113pmol/l (140-650) in case 1. All biochemical investigations including paraneoplastic antibodies, Hep B, C serology, Anti SSA/SSB antibodies and chest/abdominal/pelvic imaging were negative in all three patients.

Figure 1: Axial (A, B) and sagittal (C) images showing characteristic pattern of symmetric bilateral hyperintense signals in the dorsal columns affecting the cuneate fasciculus as well as gracile fasciculus without contrast enhancement.

<table>
<thead>
<tr>
<th>Case 1</th>
<th>Sensory ganglionopathy due to B12 deficiency</th>
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<tr>
<td>Case 2</td>
<td>Idiopathic sensory ganglionopathy with pudendal neuropathy causing fecal incontinence</td>
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<tr>
<td>Case 3</td>
<td>Idiopathic neuronopathy</td>
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Table 1: Final diagnosis
Results: SNN is a treatable peripheral nerve disorder which presents with sensory ataxia. Early diagnosis and treatment is of paramount importance to prevent disability. Underlying sinister pathologies like malignancy needs exclusion. NCS can be inconclusive initially making the spinal MRI very important in making an accurate diagnosis.

Conclusions: It is important to include sensory neuronopathy/ganglionopathy as a differential diagnosis in dorsal column lesion in addition to vitamin B12 and copper deficiency.
LONG-TERM DYNAMIC CHANGES OF NMDA RECEPTORS FOLLOWING AN EXCITOTOXIC CHALLENGE

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Background and Aims:: Excitotoxicity is the neuronal death produced by the aberrant and sustained activation of N-methyl-D-aspartate receptors (NMDARs) and the neurotransmitter glutamate. NADPH-diaphorase neurons [also known as nNOS (+) neurons] are a subpopulation of aspiny interneurons, largely spared in excitotoxic conditions. Previous findings from our group have indicated that, unlike nNOS (-) cells, nNOS (+) neurons lack the production of reactive oxygen species (ROS) in response to NMDAR activation. This is a critical divergent step in the excitotoxic cascade; however, additional mechanisms underlying the reduced vulnerability of nNOS (+) neurons to NMDAR-driven neuronal death have not been explored.

Methods:: This study evaluated the functional, genetic, bioinformatics, and molecular events related to NMDAR activity in cultured striatal nNOS (+) neurons challenged with an excitotoxic stimulus.

Results:: nNOS (+) neurons exhibited fewer but fully operational NMDARs, nNOS (+) cells undergoing chronic exposures to excitotoxic hits failed to respond to NMDA after a second challenge produced 16-20 hours after. The downregulation was limited to the distinct and selective activation of NMDARs. No changes were found in response to AMPA agonists or depolarizing conditions set to activate voltage-sensitive calcium channels. This data set indicates that nNOS (+) neurons exhibit highly dynamic responses upon variable excitotoxic conditions.

Conclusions:: Our results indicate intriguing plasticity levels and the presence of dynamic control of NMDAR activity in the subset of striatal neurons that show the abundance of nNOS synthase.
Background and Aims:: Cerebral amyloid angiopathy (CAA) is a cause of spontaneous intracerebral hemorrhage, occurring in normotensive elderly subjects. Ischemic micro or macro lesions or vascular leukopathy are frequently found on magnetic resonance imaging (MRI), supporting this hypothesis of CAA.

Aim: To report that CAA can be revealed by mild head trauma in a normotensive elderly subject.

Methods:: We report the case of a patient who was treated in the neurology department of the Principal military hospital Tunis. He consulted for heaviness of the left hemisphere and dysarthria following a head injury.

Results:: A 72-year-old man, with a history of dyslipidemia, was referred to our hospital for left hemispheric heaviness with dysarthria of abrupt onset 3 days after a mild head injury. Clinical examination showed fluctuant temporoparietal disorientation, dysarthria, total and proportional left hemiplegia including the face and left hemi hypoesthesia. CT scan showed 2 intracerebral hematomas, one in the right fronto-parietooccipital and the other in the right temporal regions. FLAIR weighted images revealed a grade 2 Fazekas leukoaraiosis. T2* weighted images in addition to the 2 intracranial hematomas, 2 subcortical microbleeds of left occipital location.

Conclusions:: CAA is a cause of hematoma and ischemic stroke. In normotensive elderly patients, the possibility of a CAA-related hemorrhage should be considered in the presence of a lobar or subcortical hematoma.
Background and Aims:: Hypertrophic pachymeningitis (HP) is a rare entity characterized by inflammation and thickening of the dura mater leading to varied manifestations. We sought to characterize the clinico-radiological spectrum and treatment outcomes in hypertrophic pachymeningitis.

Methods:: It was a single center retrospective study conducted at a tertiary care center in India. A keyword search of “pachymeningitis” was carried to identify patients diagnosed to have HP admitted during the period of 2015 to 2020. Details of clinical, laboratory, radiological, treatment profile and outcomes both clinical as well as radiological were gathered.

Results:: A total of 31 patients were identified out of which 18 were classified to have idiopathic HP. Mean age of onset of symptoms was 40.6±15.7 years. Headache was the most common symptom irrespective of etiology (27/31, 87%). Majority of the patients had multiple cranial nerves palsies (26/31, 83.8%). Oculomotor nerve was the most common nerve involved (21/31, 67.7%). Presence of constitutional symptoms and extra neurological involvement was seen in secondary HP. On imaging, focal thickening of the duramater was seen in 70.9% of the patients. Cavernous sinus and tentorium cerebelli were the most common sites of involvement (22/31, 70.9%; 18/31, 58.1%). Steroids were given in all but one patient. More than half of the patients (58.1%) had complete resolution of symptoms with treatment.

Conclusions:: Hypertrophic Pachymeningitis is a clinically heterogeneous entity. Headache and cranial dysfunction are the most common symptoms. One should thoroughly evaluate for systemic involvement as it can help to delineate the etiology. Empirical ATT should not be given blindly.
ROLE OF QUERCETIN IN ATTENUATED CARDIO-PROTECTIVE EFFECTS OF ISCHEMIC POST-CONDITIONING IN STZ INDUCED HYPERGLYCEMIC RAT HEART

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Background and Aims: The cardio protective effects of Ischemic Post-Conditioning (IPOC) are abrogated in Hyperglycemic condition. The present study has been designed to investigate the effects of Quercetin in abrogated cardio-protective effect of IPOC against I/R injury in hyperglycemic rat heart.

Methods: Six groups were employed in the present study and each group comprised seven animals. The experimental duly approved by IAEC and protocol no. is 50. Hyperglycemia induced by Streptozotocin (50mg/kg/i.p). Quercetin pretreated (100mg/kg/day, orally) for 7 days and Quercetin (10µm) perfused for 8 min in hyperglycemic rat. I/R Injury induced by 30 min global ischemia followed by 120 min reperfusion. Myocardial Injury was assessed by Lactate dehydrogenase (LDH), and creatine kinase isoenzyme (CK-MB), coronary flow rate (CFR) and Infarct size. Moreover, oxidative stress was measured by estimation of TBARS, SOD and reduced form of GSH.

Results: The level of glucose, oxidative stress and myocardial injury were significantly increased and coronary flow rate significantly decreased in hyperglycemic rat heart subjected to I/R. The IPOC afforded cardio-protection in normal rat heart. However, the IPOC mediated cardio-protection against I/R injury was markedly abolished in hyperglycemic rat heart. Quercetin treatment significantly restored the abrogated cardio-protective potentials of IPOC in hyperglycemic rat heart subjected to I/R as assessed in term of reduction in myocardial infarction, TBARS, LDH, CK-MB level, infarct size and increased SOD, GSH and CFR.

Conclusions: Treatment with Quercetin for oral and perfusion markedly restored the cardio-protective potential of IPOC in hyperglycemic rat hearts may be due to the downregulation of NF-kB and over activation of ROS.
RIColinostat induces microtubule acetylation and neurite regeneration in cellular models of diabetic and chemotherapy-induced neuropathy

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Background and Aims:: Peripheral nerves have unique regenerative capability, but two questions are still unanswered: what are the underlying mechanisms and why do some patients show higher spontaneous nerve fibers regeneration than others. Here we investigated if microtubule posttranslational modifications (PTMs) impact on neuronal regeneration in in vitro models of small fiber neuropathy (SFN) and predict intra-epidermal nerve fibers regeneration density (IENFD) in patients.

Methods:: We used differentiated F11 cells to mimic either diabetic- or chemotherapy-induced neuropathies. We challenged cells with Ricolinostat (ACY-1215), an inhibitor of HDAC6, and evaluated neurites length and microtubule PTMs. Confocal microscopy assay was performed to investigate acetylated and tyrosinated tubulin positive intra-epidermal nerve fibers, reflecting mechanical stress resilient and dynamic microtubules, respectively, in baseline and follow-up skin biopsies from SFN patients.

Results:: In F11 cells, glucose overload or chemotherapy drugs treatment impacted on microtubule organization and induced neurites shortening. Ricolinostat inhibited HDAC6 activity leading to a significant increase of acetylated microtubules, which allowed microtubule regrowth and neurites regeneration. In agreement with these findings, baseline biopsies of SFN patients showing improved follow-up IENFD revealed 2-fold increase of acetylated positive/PGP9.5 negative fibers compared to patients with worsened innervation density.

Conclusions:: Our results show that ricolinostat-induced microtubule acetylation is associated to neurite regeneration in F11 cells and that acetylated positive/PGP9.5 negative skin fibers could predict fiber regeneration in patients. These findings could drive innovative strategies of intervention in which ricolinostat administration can modulate microtubule acetylation and induce neuroprotective effects in diabetic or chemotherapy-treated patients.
CARDIOPROTECTIVE POTENTIAL OF HESPERETIN ISCHEMIC PRECONDITIONING AGAINST ISCHEMIC REPERFUSION INJURY IN RAT HEART

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Background and Aims:: Worldwide, Coronary heart disease (CHD) is the leading cause of mortality which reduced the quality of healthy human life. The present study has been designed to investigate the cardioprotective role of hesperetin with ischemic preconditioning (IPC) against ischemic reperfusion injury in rat heart.

Methods:: There was five group in the present study and each group comprises six rat. The protocol was duly approved by IAEC Reg. No. USPS/IAEC/CPCSEA/2020/Protocol No. 47. In Ischemia/Reperfusion (I/R) injury, 30 min of ischemia followed by 120 min of reperfusion produced myocardial injury which diagnosed in terms of elevated level of lactate dehydrogenase (LDH) and creatinine kinase-myocardial band (CK-MB) in the coronary effluent. In addition, the increase level of thiobarbituric acid reactive substances (TBARS), decrease level of superoxide dismutase (SOD) and reduced glutathione (GSH) was the clear indicators of oxidative stress.

Results:: I/R Injury induced myocardial damage and oxidative stress by significantly increased LDH, CK-MB, Infarct size, coronary flow rate and oxidative stress. In the present study, IPC comprised four episodes of ischemia followed by reperfusion (5 min each) and treatment with Hesperetin (100mg/kg, oral gavage) showed the cardio-protection which were assessed by reduced release of LDH and CK-MB, Infarct size, coronary flow rate and oxidative stress against I/R injury.

Conclusions:: Treatment with Hesperetin-IPC showed cardio-protective potentials in the present study may via activation of phosphatidyl inositol-3 kinase-Akt/protein kinase B and endothelial nitric oxide synthase.
RESEARCH ON THE MECHANISM OF WUZI YANZONG PILL EXCLUDING FOLIC ACID INTERFERENCE IN THE PREVENTION AND CONTROL OF NEURAL TUBE DEFECTS

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Background and Aims:: Wuzi Yanzong Pill (WYP) has a potential prevention effect on neural tube defects (NTDs) Mice, but the mechanism is not clear. To determine the content of FA in WYP, compare the effect of FA and WYP which eliminate the interference of FA and research on its mechanism.

Methods:: LC-MS was used to determine the content of FA in WYP. The pregnant mice were divided into normal group, model group, FA group and WYP group, drug intervention was given at the same time. NTDs model was established by atRA at 7.5 days of pregnancy. The levels of PI3K, Akt, P-Akt, Nrf2, Bax and Bcl-2 were detected by Western Blot.

Results:: Compared with the model group, the neural tubes in FA group, WYP group closed obviously (P<0.05 and P<0.01 respectively), while the apoptosis rate decreased significantly (P<0.05 and P<0.01 respectively). The expressions of p-Akt and Bcl-2 increased after FA treatment (P<0.05 respectively), while the content of Bax decreased (P<0.05). After WYP intervention, the levels of PI3K, p-Akt, Nrf2 and Bcl-2 increased (P<0.01, P<0.01, P<0.01 and P<0.01 respectively), but the Bax showed the opposite trend (P<0.01). The preventive effect of WYP is better than FA.

Conclusions:: WYP which eliminate the interference of FA can effectively reduce the incidence of NTDs, which may be related to the PI3K/Akt signaling pathway. (NNSF of China 81703978 and 81102552, Central Government Guided Local Funding Projects for Science and Technology Development YDZX20201400001483,Returned Chinese Scholars Technology Activities Preferred Project, Shanxi Province of China 202000026.*corresponding authors: Prof. C.G. Ma or Prof. Z. Chai)
CEREBRAL AMYLOID ANGIOPATHY-RELATED INFLAMMATION DURING BEVACIZUMAB TREATMENT FOR METASTATIC CERVICAL CANCER

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Background and Aims:: Bevacizumab is an anti-angiogenic monoclonal antibody targeting Vascular Endothelial Growth Factor (VEGF). Bevacizumab inhibits cancer angiogenesis fundamental for either cancer development, its exponential growth, or metastatic spread.

Methods:: A 72-year-old woman with metastatic cervical cancer presented a worsening confusional state after 6 cycles every three weeks of chemotherapy (cisplatin, paclitaxel, bevacizumab) and following two maintenance bevacizumab administrations. MRI showed bilateral temporo-parieto-occipital hyperintensity with numerous cortical microbleeds suggestive of a Cerebral Amyloid Angiopathy-Related Inflammation (CAARI).

Results:: Patient’s blood pressure values were normal as well as routine blood tests, autoantibodies, onconeural antibodies, and virology screening. Bevacizumab was interrupted and intravenous methylprednisolone (120 mg/day for 7 days) was started, followed by oral prednisone (25 mg/die with gradual reduction during two weeks) leading to rapid improvement of symptoms and a remarkable reduction of MRI lesions. Gadolinium-enhanced lesions have never been observed on MRIs at any timepoint. The patient resulted to be heterozygote (ɛ3/ɛ4) for apolipoprotein-E ɛ4 that increases the risk of sporadic Cerebral Amyloid Angiopathy (CAA) characterized by beta-amyloid accumulation and fibrinoid necrosis in cerebral vasculature leading to micro/macrohemorrhages and dementia. The subsequent 2-year oncologic follow up was negative for both recurrence and metastasis.

Conclusions:: To our knowledge, this is the first report on CAARI development during bevacizumab treatment. Inhibition of VEGF, which has anti-apoptotic, anti-inflammatory and pro-survival effects on endothelial cells, impair their regenerative capacity and increases expression of proinflammatory genes leading to weakened supporting layers of blood vessels and, hence, to damaged vascular integrity. In our patient, bevacizumab could further increase permeability of cerebral microvasculature likely impaired by an underlying, asymptomatic CAA.
CLINICAL OUTCOME OF YOUNG AND MIDDLE-AGED PATIENTS WITH FIRST-EVER ISCHEMIC STROKE

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Background and Aims:: Prognostic evaluation of ischemic stroke (IS) outcome is of great clinical importance because of the increasing number of young and middle-aged IS patients with unfavorable outcome on the 3rd month. Aim: To assess the outcome of young and middle-aged patients with first-ever IS on the 3rd month

Methods:: A prospective study of 101 patients with first-ever IS, admitted to the Neurology Clinic of University Hospital Pleven from 2019 to 2020 was done. The patients were subdivided into two groups: Group A of young patients aged 18-44 years and Group B middle-aged 45 – 59 years. Clinical outcome was assessed on the 3rd month as favorable (modified Rankin scale; mRs 0-2) and unfavorable (mRs 3-5). The statistical analysis was performed with the Statistical Package for Social Sciences version 24.0.

Results:: Although male gender prevailed in both of the groups, it was not found statistically significant (p=0.060). Middle-aged patients (n=75) had higher rates of risk factors: arterial hypertension (88,0%), diabetes (29,3%), dyslipidemia (65,3%) and smoking (73,9%), but the majority of them (64%) showed favorable outcome (mRs 0-2). Though young patients (n=26) tended to have lower rates of risk factors, 69.2% demonstrated unfavorable outcome on the 3rd month (mRS 3-5), found statistically significant (χ²=3.631, df=1, p=0.003).

Conclusions:: Our data demonstrate a poorer outcome of younger IS patients on the 3rd month compared to the middle-aged ones, that implies the necessity of future studies on some rare risk factors and effective therapeutic prevention.
CLASSIFICATION OF EYE CONDITION BASED ON ELECTROENCEPHALOGRAM SIGNALS USING EXTREME LEARNING MACHINES ALGORITHM (ELM)

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Background and Aims:: Electroencephalography or EEG signals is a biosignal that is rife in current research topics. EEG signals have many benefits such as the detection of epilepsy, sleep disorders, or input in a computer application. One input that can be detected based on EEG signals is the state of the eye. However, to be used as input in an application a classification with adequate performance is required. Therefore a study was conducted in which one method of learning Artificial Neural Networks, Extreme Learning Machine (ELM) will be implemented to classify eye conditions based on EEG signals.

Methods:: The dataset used to train and test the model is an eye-state dataset donated by Oliver Roesler combined with a dataset from the University of California repository website, IrvineI (UCI). There are seven corpus which consist of EEG recording done to four different people, then one corpus is added, which is a combination of all other corpus.

Results:: From the test results it was concluded that ELM can be used for the classification of eye conditions with an accuracy of 97.95% with training time of only 0.81 seconds if each data is used separately, whereas the merging of the whole dataset only reaches an accuracy of 78.94% with 5.71 seconds training time.

Conclusions:: By getting a model with good accuracy with training time that tends to be fast, the ELM algorithm can be utilized as a Brain-computer Interface by previously conducting training based on the person's EEG signal with a short amount of time to build the model.
Background and Aims:: Transient global amnesia (TGA) is a rare and benign amnesic syndrome. It manifests as a sudden onset of anterograde amnesia that spontaneously resolves within 24 hours. It affects middle-aged people between the fifth and seventh decades of life. This study discussed the proposed mechanisms, clinical and radiological characteristics of TGA.

Methods:: We report the cases of three patients who presented an episode of TGA.

Results:: The three patients were aged 64 years (case 1), 59 years (case 2) and 54 years (case 3). Two of them were males. Their medical history includes depression (case 1 and 2), arterial hypertension (case 2), type-2 diabetes mellitus (case 3). They suddenly developed acute onset of disorientation to time and space but they remained conscious. Their memories prior to these episodes were fully preserved. Accordingly to their families, an emotional trauma had preceded the episode in two cases. Symptoms gradually and spontaneously resolved over the course of 14 hours (case 1) and 6 hours (case 2 and 3). No focal abnormality was noted on neurological examination except for lacunar amnesia. Brain MRI was normal in two patients and revealed hippocampal DWI (diffusion-weighted imaging) lesions in one patient.

Conclusions:: MRI findings can support the diagnosis of TGA and may be particularly valuable in situations of low clinical certainty. It is considered a useful adjunct to the diagnosis of TGA, when performed with a minimum delay of 20 hours.
NEUROFIBROMATOSIS TYPE 1 PRESENTING AS PROGRESSIVE PROXIMAL MUSCLE WEAKNESS: AN UNCOMMON PRESENTATION MIMICKING PROXIMAL MYOPATHY

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Background and Aims:: There are three clinically and genetically distinct forms of neurofibromatosis (NF), NF type 1, type 2 and schwannomatosis. The hallmarks of NF type 1 are the multiple café-au-lait macules and associated cutaneous neurofibromas. There are various causes for generalized muscle weakness in neurofibromatosis. But progressive proximal muscle weakness is rare in NF type 1. We present an unusual case due to neurofibromas in multiple nerve roots and nerve plexuses.

Methods:: A 27 year old female presented with progressive proximal muscle weakness in both lower limb and upper limbs over one year. Her family history was unremarkable. She did not have features of connective tissue disorders or features of endocrine abnormalities. Examination revealed waddling gait, MRC grade 4 proximal muscle weaknesses in both upper and lower limbs without sensory impairment. She has multiple café-au-lait macules on her back and axillary freckles. No cutaneous neurofibromas or iris Lisch nodules were detected.

Results:: Basic blood and urine investigations and the inflammatory markers were within normal values. Serum creatine phosphokinase level was normal. The EMG was normal with no myopathic changes. Her MRI pan spine showed multiple neurofibromas and plexiform neurofibromas involving almost all neural nerve roots in varying sizes including both brachial and lumbosacral plexuses. MRI brain did not show bilateral cerebellopontine angle shwanomas. Her pure tone audiogram was normal.

Conclusions:: NF 1 presenting as progressive proximal muscle weakness without sensory signs mimicking a myopathy is exceptionally rare. Neurofibromas involving the nerve plexuses and roots are the cause and appropriate neuro-imaging confirms it.
TRACE AMINE-ASSOCIATED RECEPTORS AND ADULT NEUROGENESIS

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Background and Aims:: Trace amine-associated receptors (TAARs) are a class of sensory G protein-coupled receptors that detect amines, products of decarboxylation of amino acids. The majority of TAARs (TAAR2-TAAR9) have been described in the olfactory epithelium and considered to be olfactory receptors sensing innate odors. However, there is evidence that one of the members of this family, TAAR5, is expressed also in the limbic areas of the brain receiving projection from the olfactory system and involved in the regulation of emotional behaviors.

Methods:: In this study, we further characterized a mouse line lacking TAAR5 (TAAR5 knockout, TAAR5-KO mice) that express beta-galactosidase mapping TAAR5 expression.

Results:: We found that in TAAR5-KO mice the number of dopamine neurons, the striatal levels of dopamine and its metabolites, as well as striatal levels of GDNF mRNA, are elevated indicating a potential increase in dopamine neuron proliferation. Furthermore, an analysis of TAAR5 beta-galactosidase expression revealed that TAAR5 is present in the major neurogenic areas of the brain such as the subventricular zone (SVZ), the subgranular zone (SGZ), and the less characterized potentially neurogenic zone surrounding the 3rd ventricle. Analysis of neurogenesis by using specific markers doublecortin (DCX) and proliferating cell nuclear antigen (PCNA) revealed a 2-fold increase in the number of proliferating neurons in the SVZ and SGZ of TAAR5-KO mice, but no such markers were detected in mutant or control mice in the areas surrounding the 3rd ventricle.

Conclusions:: These observations indicate that TAAR5 is not just providing olfactory input into limbic brain areas but is also involved in processes related to adult neurogenesis.
AN OBSERVATIONAL ANALYTICAL STUDY OF PATIENTS WITH CEREBRAL VENOUS SINUS THROMBOSIS (CVST) TO IDENTIFY CRITICAL PROGNOSTIC FACTORS IN SOUTH COASTAL STATE OF KARNATAKA INDIA

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**Background and Aims::** Background CVST presents with a wide variety of neurological symptoms in various combinations and has a high mortality up to 50%. Recent advances in neuroimaging and therapeutic interventions have brought it down to 20% AIM To identify critical prognostic factors associated with poor outcome in patients with CVST.

**Methods::** Methods All cases of CVST of both genders and age >18y from July 2015 to July 2020 who were not terminally ill and bed ridden were evaluated at entry point for various risk factors and after 30days for outcome assessment with Modified Rankin Scale (mRs). Outcome is dichotomized applying mRs <3 as good outcome and analyzed with chi Square test or Fischer exact test in a bivariate analysis to identify associated variables.

**Results::** Results A total of 149 subjects were studied and GCS <9(p<0.001), focal neurological deficits (p-0.05), presence of mass effect (p-0.001) and the need for decompressive hemicraniectionomy (p-0.001) were associated with poor outcome. Age, gender, diagnostic delay, seizures at onset, papilledema, parenchymal lesions, deep sinus involvement and multiple sinus thrombosis were not associated with poor outcome.

**Conclusions::** Conclusion In present era, Early diagnosis and therapy of patients with CVST is associated with a favorable outcome in the face of conventional risk factors except four critical factors.
Background and Aims:: People who care for patients affected by neurocognitive disorders are at increased risk of developing stress and burnout. The workload has experienced a notable increase during the pandemic. In our observational study, we assessed the presence of anxiety, burnout and compassion fatigue in caregivers (family members and health professionals (HCW)). We also evaluated the presence of mental disorders as well as anxiety and depressive disorder.

Methods:: We recruited 67 caregivers (41F; 26M; mean age 43.63 years) (family members and health workers) of elderly people in residential rehabilitation facilities or observed in an outpatient office. Observation period: February-March 2021. All caregivers were administered the following scales: ProQoL; CBI. The SAVE-9 scale was used for the assessment of anxiety and work stress in viral pandemic.

Results:: The data obtained showed a significant increase in all mean scores of anxiety and burnout in pandemic periods. Family caregivers have higher scores on the CBI scale and lower scores on the Satisfaction Compassion subscale of ProQoL than other HCW; nurses had higher scores on ProQoL and CBI (31.37% on the ProQoL Secondary Trauma subscale). SAVE-9 scale showed high percentage scores in all factors (Total mean score: 21.10; 55.22%; Factor I: 13.91; 52.23%; Factor II: 7.19; 64.17%).

Conclusions:: The COVID-19 viral pandemic is having a major impact on the psychological and occupational well-being of caregivers of people with Alzheimer’s disease. However, family caregivers have a greater burden of work-stress. Our small study confirmed this incidence observed in previous studies, also highlighting high levels of anxiety and stress in HCWs.
LONG DURATION PROGNOSIS OF HYPERTROPHIC PACHYMENINGITIS

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Background and Aims:: The aims of this study is to reveal details of long-term treatment and prognosis of hypertrophic pachymeningitis (HP).

Methods:: We investigated 10 HP patients experienced in our hospital from April 2015 to June 2020. As a diagnostic criterion for HP, the patient presented with some neurological symptoms and showed abnormal dural thickening by MRI Gd enhanced T1 weighted image.

Results:: The results of these 10 HP cases were as follows; the average age of onset was 61.5 years(range 29-79), four males and six females, underlying diseases (idiopathic 3 cases, ANCA-related vasculitis 3 cases, Aspergillus infection 2 cases, IgG4-related disease 1 case, ulcerative colitis 1 case), part of dural thickening (only supratentorial 6 cases, including infratentorial 4 cases), the form of dural thickening (linear type 6 cases, nodular type 4 cases), headache in 7 cases, pyrexia in 3 cases, lesion part of cranial nerve (upper cranial nerve 7 cases, lower cranial nerve 3 cases), maximum PSL dose 0.79 mg/kg/day, PSL maintenance daily dose 0.18 mg/kg/day, only 2 cases could end immunotherapy, 3 cases of the immunosuppressive drug combination, mRS decreased from 3.1 to 1.4 before and after treatment, Some sequelae remained in 8 cases, recurrence occurred in 3 cases, and 2 cases died.

Conclusions:: Idiopathic HP and HP associated with immune disorders responded to steroids and immunosuppressive drugs and recovered well, but it was difficult to terminate steroids. Secondary HP associated with Aspergillus infection could not use steroids pathologically, and recovery was poor.
RELATIONSHIP OF TNF-Α AND CRP WITH ELECTRONEUROPHYSIOLOGICAL PARAMETERS IN PERIPHERAL DIABETIC NEUROPATHY PATIENTS

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Background and Aims:: Diabetic peripheral neuropathy (DPN) is the most common complication of diabetes mellitus type 2 (DM2). The mechanisms of inflammation can damage effect on the nerve fiber. Aim was to assess the relationship between the inflammatory markers TNF-α, CRP and electroneurophysiological (ENMG) parameters depending on the duration of DPN.

Methods:: 76 patients with DM2 were evaluated (target HbA1c level <8%). The mean age was 62.6 ± 0.7 years, the duration of DM2 was 6.8 ± 0.5 years. There were two groups depending on the duration of the PDN: 1 (n = 34) - less than 2 years, 2 (n = 34) - more than 2 years. We used the American Nicolet Viking IV for a quantitative assessment of the speed of conduction along the nerve. TNF-α and CRP was carried out using immunological methods.

Results:: There was a speed decrease of the motor and sensory peripheral nerves. The conduction was significantly lower in group 2 (p <0.05), with more severe damage to the motor fibers. Correlation analysis showed a direct relationship between CRP and nerve conduction velocity (p <0.05) in both the 1 and 2 groups. Similar changes were revealed between TNF-α and the sensorimotor dysfunction according to ENMG, a direct relationship was noted between TNF-α and the speed of conduction along the nerve (p <0.05) both in the 1 and 2 group.

Conclusions:: The high level of inflammation markers TNF-α, CRP in patients with DM2 and a long history of DPN confirms the hypothesis of a possible contribution of nonspecific inflammation to the development of neuropathy.
AN INTERESTING CASE OF CEREBRAL AVM

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Background and Aims:: Vascular malformations in brain can present with varied symptoms like focal or generalised seizure, severe headache, focal neurological deficits and sudden loss of consciousness. Approximately one-third to one-half of patients with newly diagnosed previously unruptured brain Arteriovenous Malformations(AVM) present with seizures. One percent of unprovoked first seizures are caused by brain AVMs.

Methods:: A 52 years old post-menopausal female with emotionally grief condition and prolonged crying due to loss of a family member came with complaints of sudden focal seizure without aura or automatism involving right upper limb and lower limb with deviation of head towards right side, tonic in nature, lasting for 2 minutes with impaired awareness without any postictal weakness or confusion, with no previous history of seizures or any comorbidities.

Results:: MRI Brain showed cluster of multiple T2 flow voids in left frontal region measuring 5.2*5.3 cm without surrounding edema & mass effect suggestive of Arterio-Venous Malformation in left frontal lobe (Spetzler-Martin grading 2) (Bag of black worms appearance).

Conclusions:: The mass effect of the brain AVM nidus or associated venous pouches may be responsible for triggering seizure activity. First focal seizure whether its provoked or unprovoked, irrespective of age, sex and systemic comorbid condition and previous normal neurological status, necessitates detailed and urgent neuro-imaging to rule out major life threatening causes of any etiology like vascular, neoplastic, infective, inflammatory, immune mediated, CSF flow disorders and congenital anomalies in brain.
A STUDY OF USING BARIA ZASAL THERAPY AS A TREATMENT METHOD OF CONCUSSION

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Background and Aims:: In Traditional Mongolian medicine the baria zasal therapy has been inherited for hundreds of years due to the Mongolian lifestyle and nomadic culture. TMM's Baria zasal therapy hasn't lost it's value even the modern medicine, developing rapidly nowadays and still using as a main treatment of concussion. To study the factors in choosing the baria zasal treatment in concussions.

Methods:: A total of 400 hundred people was surveyed in our study and asked what would they do if their child had a concussion. The questionnaire also included the demographics and religions of the respondents.

Results:: The average age of our survey respondents is relatively young (average age 35.3±9.1) and 86% (n=354) highly educated. In terms of religions 59.6% (n=186) were Buddhists and 25.8% were non-religious people(n=80). When asked to how they treated concussion at that time, 62.3% of them answered they went to the bariachi which known as massagist. Using regression analysis to study the factors to why people chose to visit bariachi it shows based on their own beliefs [OR; 95%CI=2.21; 1.23–2.63, p=0.04], based on their previous experiences (2.36; 1.38–4.03, p<0.001) were statistically true. After experiencing the concussion, there are no difference found in age, religion or education between those who chose to visit bariachi and those who did not.

Conclusions:: Most parents and guardians seek treatment from a bariachi's their first choice in when their child suffers a concussion and the choice of visiting bariachi does no depend on their age, education level or religion but on their own beliefs.
THE EFFECT OF BRACHIOCEFALIC ATHEROSCLEROSIS TO THE CEREBRAL CIRCULATION INSUFFICIENCY

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Background and Aims:: The aim of the study was to examine the structural features of atherosclerotic lesions of the brachiocephalic arteries and their relationship with the severity of cerebral circulation insufficiency.

Methods:: The study included 77 patients, 38 of them were subsequently operated on the brachiocephalic arteries, 39 were continued conservative treatment. In terms of gender, men were 67 (87.0%), while women were 10 patients (13.0%). The average age was 57.7 ± 7.8 years. Duplex scanning of blood vessels was performed using Ultramark-9 (ATL) and Sonos-1800 (Hewlett Packard) devices with sensors operating at 7-12 MHz.

Results:: The asymptomatic character of the cerebral ischemia with lesions of the brachiocephalic arteries was 29.6% of all patients included in the study. The clinic of transient ischemic attacks was revealed in 59.3% of patients included in the study (75.3% in operated patients and in 43.1% in patients receiving conservative treatment). The expediency of a comprehensive examination of patients with atherosclerosis of the branches of aortic arch has been substantiated, including a clinical assessment of symptoms and the use of additional imaging methods (duplex scanning of arteries, transcranial Doppler, computed tomography of the brain), simultaneous participation in the treatment were cardiovascular surgeons, neurologists and cardiologists.

Conclusions:: The study data indicate the role of early diagnosis of atherosclerotic lesions of the brachiocephalic arteries, which makes it possible to carry out complex measures aimed at stabilizing the course of the disease, improving the prognosis, including the timely determination of indications for surgical treatment of this disease.
CONSUMPTION OF OPIOID ANALGESICS IN THE PRIMARY HEALTH CARE IN ALBANIA, 2010-2019

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Background and Aims:: Authors discuss the use of opioid drugs (morphine, fentanyl, oxycodone, pethidine, and tramadol) in Albania, mainly at the primary health care level; and differences of prescription patterns over a period of 10 years.

Methods:: The data were assembled from Health Insurance Institute in Tirana, Albania and analyzed for the period 2010-2019. The consumption of drugs was expressed as a number of Defined Daily Dose (DDDs)/1000 inhabitants/day. We also analyzed the data of imported and domestically produced drugs, which represent the total consumption of opioid analgesics in the country.

Results:: The consumption values of opioid drugs in Albania are comparatively low. An important part of the opioid drugs flows out from the reimbursement scheme. A comparative analysis in the consumption of opioids between Albania and other countries suggested also important differences in the overall consumption values.

Conclusions:: The consumption values of opioid drugs in Albania are comparatively low. An important part of the opioid drugs flows out from the reimbursement scheme. A comparative analysis in the consumption of opioids between Albania and other countries suggested also important differences in the overall consumption values.
DIAGNOSTIC DIFFICULTIES AND CROSS-IMMUNOREACTIVITY OF PML. CASE-REPORT.

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Background and Aims:: To describe the difficulties clinical diagnosis of progressive multifocal leukoencephalopathy (PML) not associated with HIV.

Methods:: MRI, PET, stereotactic biopsy, open surgery, histology, histochemistry, immunohistochemistry, PCR.

Results:: A 70-year-old man, not suffering from HIV, had progressive neurological symptoms. Then he underwent MRI and PET-CT of the brain: differential diagnosis of multifocal autoimmune, inflammatory disease or tumor. The patient is referred for stereotactic biopsy. The biopsy was analyzed in 3 medical institutions, in some of them anaplastic ganglioglioma was diagnosed, in the other demyelinating disease, in the third PCR method excluded herpetic encephalitis, tick-borne encephalitis, borreliosis and toxoplasma. Two months after the biopsy, craniotomy was performed with the removal of one of the nodes. On histological examination, PML was diagnosed.

Conclusions:: From a clinical point of view, differential diagnosis was complicated by the absence of a confirmed cause of immunodeficiency in the patient. Difficulties in the histological diagnosis of PML in this case were due to the small volume of material in the case of stereotaxic biopsy. Also in this case, due to the activity of the viral process, a large number of large bizarre cells were identified. Particularly difficult to diagnose was nuclear cross-reactivity of large bizarre cells with antibodies to ki-67, p53, Vim and NF, due to active replication of the virus in tumor cells. Based on our clinical experience, we can assume that the spectrum of antibodies with cross-reactivity and its severity in the case of PML is dependent on the viral replication activity.
POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES) WITHOUT HYPERTENSION, A CASE REPORT

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Background and Aims:: PRES is a disorder manifested by various neurologic symptoms, such as headache, visual and consciousness disturbances, seizures and focal neurological deficits. It is associated with a number of conditions, leading to white matter edema.

Methods:: We present the case of a young woman with headache and generalized tonic-clonic seizures in the early postpartum stage.

Results::

![Brain MRI Image](image-url)
A 22-year-old woman primigravida was sent to ER after 2 episodes of bilateral tonic-clonic seizures one hour after caesarean section under spinal anesthesia at her 39-40 week of an uncomplicated pregnancy. She never smoked or consumed alcohol. On arrival, she was alert and oriented, reported occipital headache, there were no evidence of meningeal signs, neither focal neurologic deficits. Visual field testing, cranial nerve examination and vital signs were normal. Laboratory findings were significant for an elevated WBC, LDH, RF, CRP, and hyponatremia of 129 mmol/l. Urinalysis was remarkable for proteinuria, glucosuria, and the presence of WBC and RBC. Renal and hepatic function, ANA, ANCA resulted normal, as well as EEG and brain CTA. Brain MRI showed bilateral multiple cortical lesions at the frontoparietooccipital regions with signal restriction in DWI, consistent with PRES. MRI performed one week later revealed resolution of lesions. The patient's headache resolved on the 3rd day of hospitalization, no more seizures were recorded. She was discharged home with no neurologic deficits.

**Conclusions:** PRES should be always suspected in a patient which presents in the postpartum period with seizures and headache. It is essential to treat PRES promptly in order to prevent permanent neurological deficits.
THE USE OF A NEW DIAGNOSTIC METHOD IN PATIENTS FOR THE DIFFERENTIAL DIAGNOSIS OF ALZHEIMER'S DISEASE (AD)

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Background and Aims:: Selection of biomarkers incoming contact to the selected diagnostic complex is dictated by the participation of these proteins in the pathogenesis of AD, including at early asymptomatic stages of AD.

Methods:: Selected 147 patients with verified diagnosis of presenile type of Alzheimer's disease (n=17) – 1-group, senile type of Alzheimer's disease (n=30) - 2-group and chronic brain ischemia (n=100) - 3-group. Determined the dehydroepiandrosteron sulfate (DHEA-s) in blood serum of patients.

Results:: The average age of patients was 71,05±1,15 years in 1-group, 57,2±0,92 years in 2-group, 67,18±1,06 years 3-group. Determination of biomarker DHEA-s showed that the level of DHEA in 1-group and 2-group has not changed or has changed slightly, but in 3-group the level of DHEA-s increased by 2 or more times (concentration in norm - 2.6 mmol / l)

Conclusions:: The high diagnostic efficiency of biomarker was asserted, including determination of serum of patients DHEA-s for the early diagnosis and monitoring the effectiveness of therapy and to identify high-risk groups Alzheimer's disease, and chronic brain ischemia.
Background and Aims:: Typical chronic inflammatory demyelinating polyneuropathy (CIDP) is a symmetric sensorimotor polyneuropathy. We report three cases with motor predominant CIDP and phrenic nerve palsy.

Methods:: Case reports:

Results:: Case 1 : A 39-year-old woman had quadriplegia without any sensory deficit associated with areflexia and orthopnea. ENMG (electroneuromyography) showed motor demyelinating polyneuropathy with prolonged distal motor latencies of phrenic nerves. Respiratory function tests disclosed a decreased forced vital capacity (FVC). She was treated with IVIg and cyclosporine, and progressively improved after requiring non invasive ventilation (NIV). Case 2 : A 25-year-old man diagnosed as having Guillain-Barré syndrome and treated by IVIg. 4 years later he presented with worsening limb weakness and dysphonia. Examination revealed severe weakness and atrophy. ENMG testing showed abolished distal motor responses. Patient was treated with IVIg+prednisone+azathioprine. However, he developed worsening respiratory function (FVC at 30%) and later died following a bronchopulmonary infection. Case 3 : A 69-year-old male patient was admitted with progressive motor weakness. The neurological findings were symmetrical weakness with no sensory deficits. ENMG showed motor predominant CIDP. 2 years later, a flaccid quadriplegia and respiratory failure occurred, treated with tracheostomy, IVIg, azathioprine and prednisone. His clinical status slowly improved. he removed tracheostomy then remained fully independent. However, he died in 2015 of pulmonary embolism.

Conclusions:: Our patients illustrate the rarely reported association of motor predominant CIDP and phrenic nerve palsy. ENMG of the phrenic nerve and respiratory function measurement in different subgroups of CIDP patients may clarify the frequency and prevent more severe features of respiratory failure.
STROKE-LIKE EPISODES REVEALING SEVERE HYPERTHYROIDISM IN A MIDDLE-AGED WOMAN: A CASE REPORT

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Background and Aims:: We report the case of a middle-aged woman who presented to the ED with stroke-like symptoms and normal brain imaging, ultimately revealing thyrotoxicosis with severe hyperthyroidism.

Methods:: A 49-year-old diabetic woman presented to the emergency department with a 5 day history of headaches and left sided weakness. She had a similar episode 3 months prior treated as a "minor stroke" from which she had fully recovered. She reported significant weight loss (30kg) over 6 months. On examination, she had a mild left-sided hemiparesis with decreased tone, flexor plantar responses and slightly diminished deep-tendon reflexes. She had a diffuse goiter with a bruit and her hearbeat was irregular. Lab tests found hyperthyroidism with low TSH <0.005 and elevated T4 levels >100. She had 2 EKGs 24hours apart: the first one unremarkable while the second one showed atrial fibrillation.

Results:: She was hospitalized with a working diagnosis of stroke due to paroxysmal atrial fibrillation in the context of thyrotoxicosis. Subsequent brain MRI however was completely normal. Further investigations revealed markedly elevated TPO levels >1000 Ul/ml, slightly elevated anti TSHR at 2.6 Ul/ml and thyroid sonography was compatible with thyroiditis. CSF examination also found anti TPO at low levels (2.85 Ul/ml). She was started on methimazole and propanolol, with anticoagulation. Her left-sided weakness resolved completely over the next two weeks.

Conclusions:: Stroke-like episodes have been rarely described with thyroid disease, mostly in the context of Hashimoto's encephalopathy. This patient however had no seizures or altered mental status and her symptoms resolved upon treating her thyroid disease.
FULMINANT IDIOPATHIC INTRACRANIAL HYPERTENSION AND REVERSIBLE SPLENIAL LESION SYNDROME (RESLES) : A CASE REPORT

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Background and Aims:: Reversible splenial lesion syndrome (RESLES) is a rare clinico-radiological entity characterized by transient lesions involving the splenium of the corpus callosum (SCC). It has been described in a broad spectrum of conditions. We report the case of a RESLES in a young woman ultimately diagnosed with fulminant idiopathic intracranial hypertension (IIH). To the best of our knowledge, this is the first such association reported.

Methods:: A 29 year-old woman with chronic kidney disease was admitted to the emergency department with a two-week history of severe headaches, nausea and rapidly progressive vision loss. On admission, the patient had no light perception in both eyes, bilateral stage 3 papilledema and bilateral sixth nerve palsies. Brain MRI with MRV was completely normal apart from a 1 centimeter lesion of the splenium of the corpus callosum. A lumbar puncture was performed: CSF composition was normal but the opening pressure was elevated at 43 cmH2O. The rest of her workup was normal apart from elevated creatinine at 15 mg/L. She was diagnosed with fulminant IIH.

Results:: The patient underwent ventriculoperitoneal CSF shunting with initial relief of symptoms but no visual recovery. Three days later however, her headaches reappeared. A repeat MRI showed extensive cerebral venous thrombosis and the patient was started on anticoagulants. Repeat MRI at 6-month follow up showed complete regression of the splenial lesion and thrombosis.

Conclusions:: Whether a coincidence or not, we report a case of an association between fulminant idiopathic intracranial hypertension and reversible splenial lesion syndrome. The physiopathology remains unclear.
TELENEUROLOGY DURING THE COVID-19 PANDEMIC: EXPERIENCES AND CHALLENGES

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Background and Aims:: This survey aimed at providing a comprehensive assessment of the rapid implementation of Teleneurology services at University Hospitals of Leicester in England in response to the Covid-19 pandemic. The twin surveys explored the experiences of both patients and clinicians.

Methods:: A target of 10% of patients who had audio consultations in the department of neurology was set for the patients’ survey. The total number of patients was 1100 during the month of May. A simple randomised procedure was followed for patient’ selection; every 10th patient in the list was contacted by phone by the auditors.

Results:: 44% of patients rated their experience as similar to their face-to-face appointments; whilst 18% rated their experience as better. 42% (19/45) of patients would prefer a face-to-face appointment over a phone appointment as opposed to 38% (17/45) who prefer audio consultation. Clinicians identified subspecialties such as movement disorders, neuromuscular and dementia clinics as particularly challenging to conduct over the phone as opposed to headache and epilepsy clinics. When asked to rate their experience of audio clinics, no clear preference was expressed.

Conclusions:: Data from these twin surveys suggests teleneurology under the unique circumstances imposed by the Covid-19 pandemic has cautious positive reception from patients and a careful welcome from clinicians. Teleneurology is feasible and effective method for service delivery in appropriately selected patients. Careful patient selection, implementation of validated protocols and introduction of bidirectional videoconferencing would help address some of the shortcomings and enhance the experience of both patients and clinicians.
Background and Aims:: Guillain-Barré Syndrome (GBS) is an acute immune-mediated polyradiculoneuropathy with diverse clinical phenotype and functional outcome. In this study, we tried to evaluate clinical profile and outcome of GBS patients admitted in a tertiary care centre of Bangladesh.

Methods:: This prospective observational study was conducted in the department of neurology from 1st January 2016 to 31st June, 2020 in BIRDEM General Hospital. Fifty adult patients who fulfilled the diagnostic criteria of GBS admitted in the neurology department were included in the study.

Results:: Majority of the patients were male (64%). Mean age of the study population is 31.5 years ranging from 19 to 60 years. The most common presenting symptom at entry was ascending paralysis that occurred in 24 patients (48%). Twenty four (48%) patients had GBS disability score of 4 at entry. 39(78%) had GBS disability score of 4 at nadir. Diarrhea was reported in 14(28%) and respiratory tract infection was reported in 9(18%) cases. Majority of the patients had Brighton criteria level 1 certainty of diagnosis (62%) in our study. GBS variants according to nerve conduction studies were AIDP (54%), AMAN (34%) and AMSAN (12%). CSF protein was raised in 72% cases. MRC score at entry was significantly lower at entry and nadir in AMAN and AMSAN group of patients. Patients diagnosed with AMAN and AMSAN had worse outcome after 3 months.

Conclusions:: AIDP was the commonest variant in our study with comparatively good outcome. We recommend further multicentre prospective studies among patients with GBS to determine their long-term prognosis.
ALCOHOL USE PATTERNS DURING COVID-19 PANDEMIC IN INDIA: AN EXPLORATORY ONLINE STUDY

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Background and Aims:: Background: The COVID 19 pandemic and the nation-wide lockdown presented unique challenges to the population. Initial ban over sales of alcohol which was later lifted affected the availability and prices of alcohol. Combined with restriction of movement and disruption in daily routine, change in alcohol use patterns of the population can be anticipated. While studies have indicated a surge in the number of patients presenting to emergency services with alcohol withdrawal symptoms, data from healthy, non-treatment seeking population is sorely lacking. Aims: This study aimed to assess alcohol use patterns during COVID 19 pandemic in India via an online survey with participants inducted using snowball sampling technique.

Methods:: An online survey was created using Google forms. The link was shared with investigators’ associates and participants were inducted using snowball sampling techniques. Responses were obtained from 379 individuals.

Results:: Findings suggest that 65% of the participants who had consumed alcohol at least once in the previous year had continued alcohol consumption during the pandemic. More than 60% reported an increase in the money spent on alcohol consumption. While 17.5% reported problematic alcohol use and more than 30% had attempted cut-down/cessation, help/treatment seeking was extremely low. The most common reasons for continuing alcohol use during the pandemic were stress reduction and mood upliftment.

Conclusions:: These findings indicate a need for further detailed assessment of substance use and psychological issues which may influence alcohol use patterns during the Pandemic. The authors recommend adaptation of treatment services to match the changing requirements of the current situation.
IS THE PREHENSION BEHAVIOR TEST REALLY USEFUL? NORMATIVE DATA FOR THE SLIMMER FRONTAL ASSESSMENT BATTERY (FAB15)

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Background and Aims:: The Frontal Assessment Battery (FAB) is a neuropsychological screening tool for exploring executive functions at bedside and in the outpatient clinical practice. Many studies found a marked ceiling effect for the prehension behavior test (PBT, environmental dependency) in the healthy and clinical populations, which affects the psychometric robustness of the battery. Aim of the current study was to provide norms for a shortened version of the FAB without PBT (FAB15).

Methods:: The normative sample included 1,187 individuals (655 women; age, M=52.75, SD=17.07; education, M=10.55 years, SD=4.82). PBT had near-zero variance (M=3.00, SD=0.02), poor content validity (r vs total FAB score=0.01, p>0.05), and no discrimination power (item-total correlation=–0.02). Internal consistency also increased (Cronbach’s alpha=0.69 vs 0.72) when PBT was excluded. FAB15 factorial structure and reliability were assessed. Normative data were extracted using a regression-based approach according to sex, age, and education.

Results:: The factorial analysis revealed a single component (variance explained=53.80%) with strong loadings (all>0.50). Interrater (ICC=0.99) and test-retest reliabilities (ICC = 0.98) were excellent. The regression analysis showed that sex (low-educated women did worse than low-educated men), higher age, and lower education affected FAB15 score. Cutoff value and correction grids were computed.

Conclusions:: The prehension behavior is a “relative” of the grasping reflex, with an elicitation method less effective in triggering the motor response. Moreover, the observation of a ceiling effect in healthy subjects makes PBT not suitable for inclusion in a neuropsychological battery. The more severe FAB15 may successfully replace the conventional FAB.
IMPACT OF SQUARE STEPPING EXERCISES ON MOBILITY AND BALANCE IN OLDER ADULTS - AN EXPERIMENTAL STUDY

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Background and Aims:: Background: A fall is described as a life event in which an individual comes on the ground, floor which is mostly accidental in nature. During ageing, physiological changes set back many changes such as mitochondrial dysfunction and dropped hormonal production. These physiological events result in gradual decreased bone density, decreased muscle mass and strength in lower limbs. Aims: The intent of this study is to explore the impact of Square Stepping Exercise (SSE) in older adults to enhance balance and mobility to reduce fall risk.

Methods:: This is an experimental study in which (N-96) senior populations over sixty years were randomly divided into SSE and conventional exercise groups using a simple random sampling procedure. The interventions lasted for four weeks. Berg balance scale (BBS) and a Timed Up and Go (TUG) test were used to assess pre and post interventional effects.

Results:: Paired and unpaired t tests were used for statistical analysis. In SSE both balance and mobility showed statistically significant improvement (P < 0.001).

Conclusions:: Conclusion: Square Stepping Exercise has potential to serve as effective intervention among elder population with a high risk of fall.
CERVICAL MYELORADICULOPATHY WITH HYPOGLOSSAL SCHWANNOMA MIMICKING AMYOTROPHIC LATERAL SCLEROSIS

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Background and Aims:: A presentation of upper and lower motor signs without sensory impairment in multiple regions may suggest Amyotrophic Lateral Sclerosis(ALS). However, the co-existence of two or more other pathologies can give rise to a clinical picture similar to ALS. We report a case of co-existent hypoglossal schwannoma and cervical myeloradiculopathy presenting as ALS.

Methods:: A 45-year-old Sri-Lankan lady presented with slowly progressive painless right upper limb weakness for 6 months and mild left upper limb weakness for 2 months associated with muscle twitching, associated with slurred speech. Asymmetrical wasting and fasciculations were noted in upper limb proximal muscles with reduced power on right more than left. Her biceps and supinator jerks were normal with exaggerated triceps jerks and a positive Hoffman sign. Both lower limbs were hypertonic with exaggerated reflexes, without clonus or Babinski sign. Sensory examinations were unremarkable. Her tongue deviated to right side with fasciculations and wasting of the right side. Palatal movements and jaw jerk were normal. She was clinically diagnosed with possible ALS.

Results:: Electromyography showed denervation changes in deltoids and biceps with right predominance and right genioglossus muscle too showed denervation changes. Magnetic-resonance imaging revealed a right-sided hypoglossal schwannoma and degenerative disk disease with cervical cord compression.

Conclusions:: Pure motor symptoms with a mixture of upper and lower motor signs may suggest a clinical diagnosis of ALS. This case is an eye-opener to be open-minded about the presence of dual pathology as above, giving rise to a similar clinical picture, in order to avoid misdiagnosis.
AN EVALUATION OF DIGITISED NEUROFEEDBACK - THE FUTURE OF PERSONALISED MENTAL HEALTH CARE?

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Background and Aims:: Neurofeedback is a method of brain self-control via measurement of brainwaves and provision of a feedback signal. Previous literature has identified potential for neurofeedback as alternative treatment for neuropsychiatric conditions including stress and anxiety. The SPHERE tool aims to digitise neurofeedback for mobile devices. This study evaluated whether SPHERE was more effective in improving the common symptoms of stress and anxiety than the most popular alternative digital tool available.

Methods:: 39 participants were recruited opportunistically. Participants were randomly assigned to 3 groups to test either SPHERE, the widest-used digital tool or the widest-used digital tool with a pre-session artificial stressor applied. Participant heart rate was recorded pre- and post-session. 1-tailed Mann-Whitney U Tests or Welch's tests were used to assess significance between cohorts with p<0.05 denoting significance throughout.

Results:: A significantly larger decrease in heart rate pre- and post-session was observed amongst the SPHERE cohort compared to both other cohorts: 11.6% decrease for SPHERE, 3.02% increase for the widest-used digital tool and 1.72% decrease for the widest-used digital tool with a pre-session artificial stressor applied (p<0.01).

Conclusions:: SPHERE's digitised neurofeedback tool was significantly more effective in improving symptoms of stress and anxiety compared to the widest-used alternative digital health tool ± pre-session artificial stressor applied, indicating the benefits of accessible neurofeedback therapy. More investment is necessary in comparing digital therapies to pharmaceutical treatments for stress and anxiety and for exploration of net changes in brain frequency pre- to post-session to enhance the effectiveness of this tool.
Background and Aims:: Idiopathic intracranial hypertension (IIH) is a disorder typically affecting young and obese women. It may be associated with several pathologies. The involvement of coagulation abnormalities in the genesis of IIH remains debated.

Methods:: We report a case of a 45 years old man with a body mass index of 20.8 kg/m², followed up for IIH that was resistant to therapies. He had diffuse headaches with stage II papilledema. The intracranial pressure (ICP) was 47 cmH₂O, CSF composition was normal and so was the cerebral MRI. Two years later, the patient presented a deep venous thrombosis of the right lower limb. A complete thrombophilia work-up was performed, finding activated protein C resistance. The search for a factor V Leiden gene mutation was not performed. The patient was put on heparin therapy with a spectacular improvement of his IIH.

Results:: The association of IIH and the factor V Leiden mutation is rare; it is attributed to a prethrombotic state leading to the formation of microthrombi in the arachnoid villi reducing the reuptake of CSF and thus leading to the increase of ICP. Thrombophilia workup is requested in the setting of secondary IIH only if the patient presents episodes of thrombosis.

Conclusions:: IIH can be idiopathic or secondary (associated with different pathological conditions). Activated protein C resistance is a coagulation abnormality often linked to factor V Leiden mutation. To our knowledge, the association of IIH and factor V Leiden mutation has been reported only in 5 cases.
PECULIARITIES OF CEREBRAL HAEMODYNAMICS IN PATIENTS WITH PROLONGED DISORDER OF CONSCIOUSNESS

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Background and Aims:: Structural and functional changes of the central nervous system in patients with postcomatose prolonged loss of consciousness (PPLC) remain insufficiently studied. Aim -to study the features of cerebral hemodynamics in patients with permanent and persistent PPLC.

Methods:: A comparative examination of 34 people with persistent and 67 - with permanent vegetative state (VS) was performed to clarify the state of cerebral hemodynamics. Ultrasound duplex scanning of extra- and intracranial arteries was performed using the method of extra- and transcranial Doppler on the instrument VOLUSON 8 General Electric Med. Sist. (USA).

Results:: A dissociative character of blood supply was discovered: unlike patients with a persistent VS, in those with a permanent VS the above blood supply takes place (p≤0.05) as a result of an increased circulatory resistance in the territories of blood supply by the middle cerebral artery, common cerebral artery, vertebral artery (VA) and basilar artery (BA) with a simultaneous deceleration (p≤0.05) of the maximum blood flow in the common carotid artery (CCA), internal carotid artery (ICA) and its acceleration (p≤0.05) in VA and BA. That is, unlike patients with a permanent VS, those with a persistent VS develop functional incoordination of vascular responses, this fact manifesting an impairment of the central mechanisms of vascular tone regulation.

Conclusions:: Assessment of vascular changes in cerebral hemodynamics in permanent VS revealed a significantly higher level of disorder of regulatory mechanisms than in persistent VS. Comparative analysis of functional disorders of blood flow revealed that vascular-reflex reactions have differential diagnostic and prognostic value.