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The 18th World Congress on CONTROVERSIES IN NEUROLOGY

March 21-23, 2024 | London, UK

BOOK of ABSTRACTS

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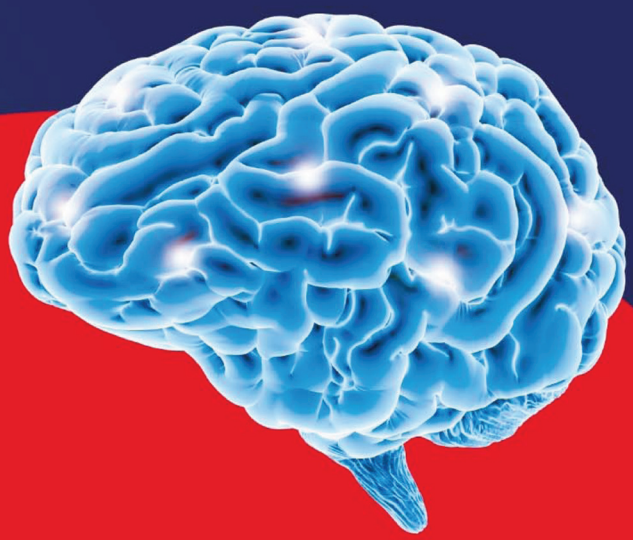
Alzheimer's Disease & Dementia



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Preventive, screening system for early detection of dementia

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Introduction: The diagnosis of dementia is often delayed, which significantly worsens the prognosis. In Hungary, there is no available artificial intelligence algorithm that could help detect early signs of dementia based on the client's digital behavioral patterns.

Method: We used the PreDEM system for the early-stage assessment of dementia. In the two pilot periods, we gathered and analyzed over 8000 test data in 3 months in 2021 and over 9200 test data in 5 months in 2023. Participants completed the following tests: short international cognitive tests and games, Stroop tests, memory games, and other cognitive games. We created a standardized evaluation system for cognitive games to compare individual game results.

Result: Our results support the effectiveness of PreDEM. There was a significant difference between the results of individuals diagnosed with dementia and those from the healthy population. These differences will be well illustrated by the density functions of the results from various groups that we present. One of the highly significant observations during the study period is that cognitive game engagement notably improves individuals with memory issues.

Conclusion: It can be stated that the PreDEM detected the first, otherwise imperceptible signs of dementia through artificial intelligence-based risk analysis. Early detection is vital as there's no cure; we must focus on improving conditions and monitoring through trend analysis. There is a need for preventive screening, as there is a clear correlation between preserved cognitive skills in later life stages and a reduced risk of Alzheimer's disease and dementia.

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The Influence of Apolipoprotein E ε4 and Lipid Profile on Cognitive Function in Mild Cognitive Impairment

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Objective: The aim of this study is to examine the relationship between lipid profiles including total cholesterol (TC), triglyseride (TG), high-density lipoprotein cholesterol (HDL-cholesterol), and low-density lipoprotein cholesterol (LDL-cholesterol) and cognitive function by the occurrence of the apolipoprotein E (APOE) ε4 in the community-dwelling elderly individuals with mild cognitive impairment (MCI).

Methods: The total number of subjects was 203 (77 men and 126 women) who were diagnosed with MCI from a Korean project of "Early Detection of Dementia". Aged 65-85 years were included in this analysis. The eight neuropsychological domain from the Korean version of Consortium to Establish a Registry of Alzheimer's Disease neuropsychological test battery (CERAD-K, NP) were conducted to test subjects. The lipid profiles of all subjects were measured including TC, TG, HDL-cholesterol, and LDL-cholesterol levels and the correlation between the lipid levels and the neuropsychological test scores was analyzed by the occurrence of the APOE ε4.

Result: There was significant correlation between HDL-C and Word List Recall Test (WLRT) of the neuropsychological test score in CERAD-K (NP) in the presence of APOE ε4 (WLRT/HDL-C: r=0.163, p0.05).

Conclusion: The HDL-C level might be correlated with verbal episodic memory domain in CERAD-K (NP) test in the presence of APOE ε4 in community-dwelling elders diagnosed with MCI.

Key Words; Mild cognitive impairment · Apolipoprotein E · high-density lipoprotein cholesterol · Korean version of Consortium to Establish a Registry of Alzheimer's Disease · Cognitive function

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Frontal versus temporal type memory deficit in amnestic mild cognitive impairment; predictive value in the diagnosis of Alzheimer disease using amyloid PET

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Background: Retention-deficit in verbal learning test is attributed to the medial temporal lobe dysfunction and retrieval-deficit to the frontal. We tried to determine whether memory deficit patterns (the retention-deficit amnestic mild cognitive impairment (rtn-aMCI) vs. retrieval-deficit aMCI (rtv-aMCI)) can discriminate amyloid positive Alzheimer disease (AD) from amyloid negative non-AD neurodegenerative diseases.

Method: One hundred and seventy-four MCI patients were enrolled who underwent a set of neuropsychological assessments, brain MRI and flutemetamol amyloid PET. All MCI patients were diagnosed using the Petersen criteria. They were divided into the rtn-aMCI (below -1.0SD on both delayed recall and recognition test) and rtv-aMCI (below -1.0SD on delayed recall, above -1.0SD on recognition test) based on Seoul Verbal Learning Test (SVLT).

Result: Of 174 patients, 106 were classified as rtn-aMCI group and 68 were as rtv-aMCI. There was no significant difference in the number of patients with positive β–amyloid PET scan between two groups (50.0% in rtn-aMCI vs. 47.1% in rtv-aMCI; $\chi 2$ = 0.143, p = 0.705). Forward digit span (6.06 ± 1.4 vs. 5.25 ± 1.6, p 0.001) & backward digit span (3.68 ± 1.2 vs. 3.29 ± 1.4, p 0.05) were lower in the rtv-aMCI group. Word fluency and Stroop tests were not different between them.

Conclusion: This study revealed that the temporal type memory deficit pattern in rtn-aMCI patients is not predictive of amyloid positive AD. We should be aware that temporal type memory deficit can also be observed in non-AD neurodegenerative disorders.

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Rapidly progressive dementia: defining "rapid"

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The definition of RPD is widely disputed in published cohorts. A standardized definition is needed to support multi-center studies required to inform the causes of RPD and optimize recognition and management of treatment-responsive causes. We applied the Clinical Dementia Rating® (CDR®)—a standardized, validated dementia staging tool—to diagnose RPD in patients who develop dementia (CDR ≥1) within 1 year or incapacitation (CDR ≥2) within 2 years of symptom onset. Criteria performance was evaluated in patients with suspected RPD enrolled at Mayo Clinic in Florida (MCF: Jacksonville, FL) and Washington University in St. Louis (WU: Saint Louis, MO), and compared with individuals with dementia included within the National Alzheimer's Coordination Center (NACC) dataset. 155/226 (68.6%) MCF-WU patients and 836/20418 (0.04%) NACC patients met the proposed RPD criteria, with etiologies including Alzheimer disease and related dementias, Creutzfeldt Jacob disease, autoimmune encephalitis, toxic/metabolic disruption, and primary psychiatric disorders. RPD was diagnosed slightly earlier in patients in the MCF-WU (mean±SD: MCF-WU, 0.81±0.81 years) vs NACC cohort (1.18±0.55 years; p0.001), owing to the prospective collection of patient data in a clinical setting. Rates of progression (ΔCDR sum-of-boxes/year) clearly distinguished patients with RPD from non-RPD in both cohorts (MCF-WU, 13.6±5.8 vs 4.7±5.9, p0.001; NACC, 6.7±3.1 vs. 1.7±1.4, p0.001). The proposed definition of RPD rapidly identified patients with distinct rates of dementia progression and diverse causes of RPD across multiple cohorts. Broad application of this definition may support the implementation of multi-center studies in RPD.

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Overdiagnosis of AD by using ALZAS biomarkers in absence of genetic family tree

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Nowadays; It seems to overlook the crucial role of genetic counseling within family trees by emphasizing the sole reliance on simple blood tests for ALZAS biomarkers in diagnosing Alzheimer's Disease (AD). While blood tests for biomarkers like ALZAS show promise in aiding early diagnosis, they represent just one part of a complex picture, especially within familial contexts.

Genetic counseling serves as a fundamental component in understanding hereditary patterns and potential genetic predispositions within family trees. It delves into intricate details beyond what a blood test can reveal. By examining family medical histories, genetic counselors can identify patterns of inheritance and potential risk factors for AD. They elucidate the nuances of genetic information, providing invaluable insights into the interplay between genetics and disease manifestation.

Relying solely on blood tests overlooks the intricate genetic landscape that shapes an individual's risk of developing AD. It neglects the significance of familial inheritance patterns and the diverse genetic influences that can contribute to the disease. Genetic counseling doesn't just focus on biomarkers; it offers a holistic view, encompassing environmental factors, lifestyle choices, and familial genetic nuances.

Genetic counselors offer tailored guidance, empowering individuals with information on risk mitigation strategies, informed decision-making regarding genetic testing, and psychological support through the complexities of genetic information.

In essence, while blood tests for biomarkers like ALZAS hold promise, they are just a piece of the puzzle. Genetic counseling plays an indispensable role in providing comprehensive understanding and personalized insights into AD risk within familial contexts, offering a more nuanced and holistic approach to diagnosis and management.

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Downstream Implications of Targeting Amyloid Protofibrils and Tau as a Predictive Biomarker: Results of a Clarity Subanalysis

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Background: Lecanemab is a monoclonal antibody selectively targeting soluble amyloid beta aggregated species in the brain of patients with Alzheimer's disease (AD). Tau aggregates are also involved in the pathogenesis of AD and correlate with neurodegeneration and severity of symptoms.

Objective: To present biomarker results from Clarity AD, focussing on subgroups stratified by patients' tau levels.

Methods: Clarity AD was an 18-month, double-blind study in patients with early AD or mild cognitive impairment (MCI) due to AD. Participants were randomly assigned (1:1) to lecanemab 10 mg/kg bi-weekly or placebo. Primary endpoint was change from baseline at 18 months in the Clinical Dementia Rating-Sum-of-Boxes (CDR-SB). Subgroup analysis was conducted in patients stratified by baseline tau levels.

Results: Patients included in the optional tau positron emission tomography substudy (n=342) were grouped by low (SUVr 1.06, n=141), intermediate (SUVr 1.06–2.91, n=191) and high (SUVr 29.21, n=10) tau levels. In the low tau subgroup, lecanemab reduced decline on CDR-SB at 18 months by -0.59 versus placebo (p=0.022); 60% of patients on lecanemab demonstrated improvement and 76% no decline on CDR-SB compared with 28% and 55% on placebo, respectively. In the low tau group, lecanemab showed the highest impact in the medial temporal lobe, a region of early Braak stages, while in the intermediate-high tau group, it impacted progression more broadly.

Conclusions: Lecanemab impacts tau pathology in all patients regardless of tau levels. The low tau subgroup results support earlier treatment with lecanemab.

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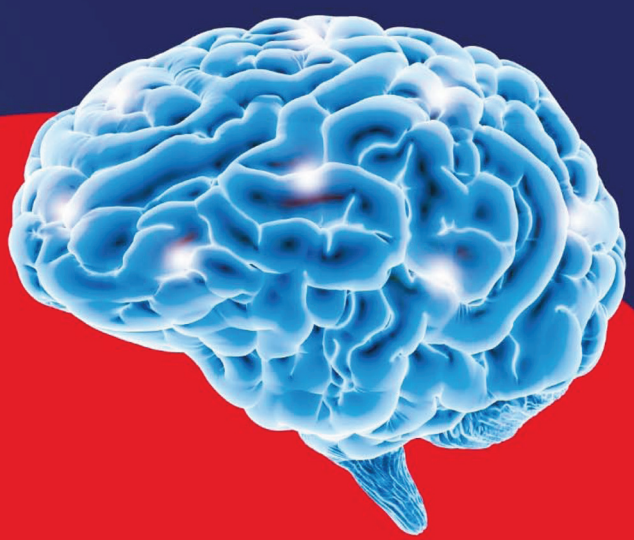
Epilepsy



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Cognitive Rehabilitation by Compensatory and Restorative Computing Training in Patients with Epilepsy and Mild Cognitive Impairment

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The study of the cognitive rehabilitation by compensatory and restorative computing training efficacy during 3 months revealed the effectiveness for epileptic patients with a significant improvement in cognitive functioning. More significant results were observed under the combined use of psychoeducation and CT, compared to the use of cognitive training only. The results of the study 12 months after CT showed that patients in study groups 1 and 2 had a level of cognitive functioning close to that at the beginning of the study, i.e. the improvement in cognitive functioning after three months of cognitive training is not sustainable without further training. There were significant differences from the indicators shown by the control group patients who did not undergo a rehabilitation program and had a more pronounced further decline in cognitive functioning, higher anxiety, and lower quality of life. Non-pharmacological correction with the use of the CT in patients with non-dementia level cognitive decline allows to slow down the progression of the latter and improve the overall mental state. The combined use of CT and psychoeducation facilitates social functioning and improves patients` quality of life, but the mechanism of psychoeducation's impact on cognitive functioning is likely to be indirect, through the reduction of anxiety and depression symptoms. Potential areas of further research include a longer follow-up period, which may provide insight into the feasibility of using such CT regularly, and/or the search for forms of daily activity that would serve as a cognitive function training.

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Movement disorders and seizures as a manifestation of systemic lupus erythematosus

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Objective: To describe a case report of a patient with systemic lupus erythematosus (SLE) presenting with congenital hearing loss, seizures, myoclonus, and dystonia.

Background: Movement disorders and epileptic seizures are possible neurological manifestations of SLE.

Method: We report the case of a 16-year-old female with congenital hearing loss diagnosed with SLE.

Results: About two years prior to presentation, the disorder started with unexplained rises in temperature, weakness, headaches, pain in small joints and muscles, and generalized tonic-clonic seizures. The patient experienced episodes of myoclonus and abnormal dystonic posturing of the left upper arm, forearm, hand, and left toe extension three months after the onset. Brain magnetic resonance imaging revealed diffuse cortical atrophy and calcification in the globus pallidus, the right thalamus, and the temporal cortex. Electroencephalography showed temporal intermittent rhythmic delta activity; antiphospholipid antibodies (aPLs) were elevated in the serum. Steroids were prescribed for SLE; valproic acid was administered for seizures and movement disorders. During a two-year follow-up period, the patient experienced only two episodes of myoclonus and dystonia, and remained seizure-free.

Conclusion: The seizures in this patient were probably related to an autoimmune-mediated pathogenesis via aPLs, while myoclonus and dystonia might also be associated with thalamic lesions. Neurological complications of SLE are common, but the coexistence of myoclonus, dystonia, and epileptic seizures in patients with congenital hearing loss and multiple morphological changes in the brain has not been reported. Awareness of this condition can improve treatment strategies and outcomes for patients, as well as optimize resources in the healthcare setting.

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Postpartum Posterior Reversible Encephalopathy presenting as Myoclonic Seizures

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Introduction: Posterior reversible encephalopathy syndrome (PRES) can present with seizures, encephalopathy, visual disturbances, headache, or focal neurologic deficits. Possible triggers include hypertension, metabolic disturbances, toxic agents, renal impairment, septic conditions, eclampsia, and preeclampsia. PRES can also develop shortly after or several weeks after delivery. Seizures. We report a case of postpartum PRES manifesting as myoclonic seizures that persisted for several months

Case presentation: A 31-year-old female several weeks after the vaginal delivery presented to the hospital with impaired consciousness, diffuse hyperreflexia and myoclonic jerks. The symptoms first started shortly after giving birth manifesting with involuntary limb movements with subsequent motor weakness, frequent falls, recurrent episodes of altered consciousness and somnolence.

At presentation, serial myoclonic seizures were observed with a frequency of 15-16 per minute. The jerks were more prominent on the right side of the body. A comprehensive laboratory investigation including the whole panel for autoimmune encephalitis and serology for infectious disorders did not disclose any abnormality. Ictal EEG demonstrated high amplitude delta waves with superimposed beta activity and T2-weighted and flair MRI revealed characteristic images for vasogenic edema:.After the admission, the patient experienced two GTCS. Trials of several ASDs were used, but clonazepam proved to be the most effective. Subsequently, the patient progressively recovered neurologic function, however, myoclonic seizures still persisted.

Conclusion: Even though PRES is considered to be a reversible condition, rarely patients develop epilepsy. In our case, the patient developed myoclonic epilepsy, which was effectively treated with clonazepam.

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Social cognition deficits affect the quality of life in patients with drug-resistant temporal lobe epilepsy

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Objective: Numerous studies indicate a significant decline in the quality of life (QoL) among patients battling drug-resistant epilepsy. It may be associated with various factors, including health, mood, or the quality of interpersonal relations. The ability to establish close and satisfying relationships is in turn related to the individual's social skills. This study aimed to evaluate the social cognition abilities of individuals with intractable epilepsy and understand how it affects QoL.

Methods: We gathered 80 adult individuals with drug-resistant temporal lobe epilepsy with the average duration of epilepsy equal 19±6,98 years and 80 demographically matched healthy volunteers. The neuropsychological assessment was conducted using a set of tests evaluating the quality of life (QOLIE-31-P), recognition of emotions (RMET), recognition of intentions based on observation of body movements (CID-5) and the level of depression and anxiety (HADS).

Results: Individuals with epilepsy scored significantly lower across all measures of social cognition compared to healthy controls (p0.05). Further analysis highlighted a significant positive correlation between QoL scores and RMET (r = 0.61; p0.05), CID-5 (interaction recognition: r = 0.73; p0.05; interaction naming: r = 0.38; p0.05), and a negative correlation between QoL and the depression subscale of HADS (r = -0.61; p0.05).

Conclusion: Quality of life is related with social cognition deficits and depression. Patients with epilepsy should be provided with special care including the therapy of social cognitive deficits and enhancing social competences to improve their quality of life and reduce the risk of depression.

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Objective vs subjective memory deficits in patients with mesial temporal lobe epilepsy

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Purpose: Patients with mesial temporal lobe epilepsy (MTLE) present diverse profiles of cognitive disturbances. Due to the localization of the epileptic focus, the predominant deficit observed both in objective assessments and patient-reported complaints is memory impairment. Previous studies have frequently prioritized the objective evaluation of memory, neglecting the aspect of its subjective evaluation. In this study, objective assessment (testing) and subjective assessment (questionnaire-based) were combined to obtain a comprehensive understanding of the mnestic functioning of patients. Furthermore, we aimed to investigate the relationship between subjective and objective memory impairments and the severity of depressive symptoms.

Method: Twenty-eight patients with MTLE and twenty-seven demographically matched healthy individuals were examined using Wechsler Memory Scale (WMS-IV), Questionnaire of Memory Efficiency (QME) and Beck Depression Inventory (BDI-II).

Results: Patients with MTLE achieved significantly lower scores than healthy individuals in all subtests of the WMS-IV: Logical Memory I&II (p0.001), Verbal Paired Associates I&II (p0.001), Designs I&II (p0.001), Visual Reproduction I (p=0.002), II (p=0.005), Spatial Addition (p0.001) and Symbol Span (p0.001). Furthermore, patients subjectively rated their memory lower (p=0.002) and had more severe depressive symptoms (p0.001) than healthy individuals. However, no correlation was found between QME and WMS-IV subtests, nor between QME and BDI-II.

Conclusions: Patients with MTLE exhibit impaired mnestic functions. No association was found between the severity of objective deficits and the subjective assessment of memory performance. This may be due to a reduced self-awareness regarding the extent of deficits and is not associated with a severity of depressive symptoms.

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Juvenile absence epilepsy and myasthenia gravis: a case report

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Background: Juvenile absence epilepsy (JAE) is a genetic generalized epilepsy syndrome which typically starts in adolescence and is characterized by absence seizures and generalized tonic-clonic seizures (GTCS). The management and follow-up of patients affected by both JAE and myasthenia gravis (MG) may be challenging due to the potential correlation between increased MG symptoms and epileptic seizures. Anti-epileptic drugs (AEDs) which affect the neuromuscular junction's Na+ gated channels must be administered with caution.

Case presentation: We present a 43-year-old female patient with JAE who also suffers from generalized seropositive MG diagnosed at age 22. Main symptoms of MG were ptosis, nasal speech and lower leg weakness. Symptoms were managed with pyridostigmine bromide and a low dose of prednisolone. Patient has had absence seizures, as well as GTCS from the age of 17. At age 23 she had undergone thymectomy as a mean of MG treatment. At age 35 she had a worsening of absence seizures following noncompliance to AEDs. Despite prior AEDs, control of epileptic seizures was attained following the use of levetiracetam. At age 38 she was hospitalized because of the worsening MG

symptoms caused by a respiratory infection. After antibiotic and immunoglobulin treatment symptoms had regressed. Following the successful AED treatment, patient has been seizure free with MG symptoms under control.

Conclusion: This case shows that in JAE patients who also suffer from MG prudent decision making is required, which considers the best course of treatment for each condition without impacting the other. Further carefully designed studies are needed.

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Angelman syndrome - a case report

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Angelman syndrome is a rare, complex genetic disorder. Characteristic features of this condition include delayed development (noticeable by the age of 6 to 12 months), intellectual disability, severe speech impairment and problems with movement and balance which usually appear in early childhood. Most affected patients also have epileptic seizures, microcephaly and difficulty sleeping. Patients typically have a happy, excitable demeanor with frequent smiling and hand-flapping movements.

Many of the features result from the loss of function of a gene UBE3A, located on chromosome 15. Healthy individuals normally inherit one copy of the gene from each parent and both copies are active in most of the body's tissues. However, in neurons in the brain and spinal cord, only the maternal copy is active. This parent-specific gene activation is caused by a phenomenon called genomic imprinting. If the maternal copy of the UBE3A gene is lost because of a mutation, a person will have no active copies of the gene in most parts of the brain. About 70% of cases of Angelman syndrome occur when a segment of the maternal chromosome 15 containing this gene is deleted.

We present a 28 years old patient who showed signs of delayed development at the age of 6 months with later intellectual disability, severe speech impairment, myoclonus and absence seizures, as well as happy demeanor. Extensive diagnostic workup was nonremarkable so we performed next-generation sequencing genetic testing (epilepsy panel) and found a frameshift mutation, deletion of UBE3A gene, which is the cause of Angelman syndrome.

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When is VNS the best treatment solution in pharmacoresistant epilepsy caused by grey matter heterotopia – a case report

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Grey matter heterotopias are subtype of malformations of cortical development (MCDs) characterized by accumulations of neurons in abnormal locations, mainly due to impaired migration, and present a common cause of pharmacoresistant epilepsy. A resective neurosurgical treatment, in most cases after invasive monitoring (stereo-electroencephalography), is often challenging with poor results, and for some patients alternative therapeutic methods can be offered, such as neuromodulation method - Vagus Nerve Stimulation (VNS). We present a 21-year-old male patient who was referred to our center due to pharmacoresistant epilepsy. He had focal non-motor epileptic seizures with impaired awareness. MRI findings showed widespread bilateral grey matter heterotopia, more pronounced on the right side along the trigone and the temporal horn of the right lateral ventricle, in the hippocampal area, in insular and

medial part of the right parietal lobe, as well as in the left hippocampal region. Continuous video-electroencephalography (vEEG) findings were suggestive of a complex epileptogenic network involving right temporal lobe and neighbouring structures – insula, perisylvian cortex, frontal and parietal operculum. Due to MRI findings and vEEG results, as well as patient's preferences for minimally invasive surgery, VNS was implanted (closed-loop system). Following the procedure there was a 85% reduction in seizure frequency and the patient's quality of life improved significantly. Pharmacoresistant epilepsy caused by grey matter heterotopia is a complex clinical entity and each patient requires a personal approach as well as multidisciplinary treatment. Our patient presents a case with multifocal heterotopic lesions and complex epileptogenic network, with a good response to VNS stimulation.

Keywords: Grey matter heterotopia, Malformations of cortical development, Pharmacoresistant epilepsy, Vagus nerve stimulation

Declaration of patient consent: The patient has given his consent for his images and other clinical data to be reported in this case presentation.

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EEG Findings in Patients with Epileptic Encephalopathy and Continuous Spike-Wave during Slow Sleep (CSWS) among the Uzbeks

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Epileptic Encephalopathy (EE) are severe neurodevelopmental disorders marked by refractory seizures and cognitive impairment. This study investigated EEG findings in patients with these conditions in Uzbekistan, aiming to unravel patterns and variations in the local population.

Materials and Methods: A retrospective analysis was conducted on EEG data from diverse patients with confirmed diagnoses of Epileptic Encephalopathy. The study encompassed various age groups and genders, with EEG examinations performed at Tashkent Medical Academy between 2005 and 2021. A total of 521 children, ranging in age from 3 months to 14 years, were included in the analysis. Recordings were scrutinized for characteristic abnormalities associated with Epileptic Encephalopathy. Attention was given to identifying links between EEG change and level of cognitive decline.

Results: Preliminary findings revealed a spectrum of EEG abnormalities with varying severity and distinct age-related patterns. Burst-suppression and hypsarrhythmia were prevalent in younger age groups with EE (34%), while multifocal epileptiform discharges (2%) and continuous spike-wave patterns during slow-wave sleep were prominent in older patients (47%). The CSWS pattern was notably linked with the most significant changes in cognitive function among the studied population.

Conclusion: This research enhances our understanding of EEG abnormalities associated with Epileptic Encephalopathy and CSWS in Uzbekistan. The association of CSWS with pronounced cognitive changes, may have implications for refining diagnostic criteria and developing targeted treatments. Further investigations into genetic, environmental, and therapeutic factors are warranted to optimize the management of these conditions in the local population.

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Application of combined psychodynamic treatment of idiopathic temporal lobe epilepsy (clinical case)

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Idopathic temporal lobe epilepsy has a studied overlap with affective dysregulation.

At the same time, the use of symptomatic medications, in particular antidepressants, does not affect the course of attacks. Our experience allows us to recommend a combination of antiepileptic drugs and psychodynamic psychotherapy as the most effective method of treatment.

A clinical case: Patient K, 25 years old

The attacks began at the age of 14, when the patient was taking substances to reduce weight. The substance included stimulants. Against the back-

ground of the use of substances for weight loss, the patient developed generalized tonic-clonic seizures. The MRI data showed no pathology, the EEG pattern corresponded to the diagnosis of temporal lobe epilepsy. Attacks continued after the weight loss substance was discontinued. Attacks were not controlled by antiepileptic drugs for 5 years. The patient could not study or work, hardly left the house and had suicidal ideas and was also overweight. During the treatment of antiepileptic drugs, the patient immediately received psychodynamic psychotherapy, as in the case of a psychosomatic disorder. The K's personal history included situations that led to tension and rigidity of affect, the development of impulsivity, and increased aggressiveness. Understanding the mechanism of formation of the attack became a key opportunity for changes in the experience of conflict situations. This led to a stabilization of attack control. Psychotherapy lasted 5 years. The patient has no seizures at present. During this time, she got married, gave birth to a healthy child, and works successfully.

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A report on a case of late infantile neuronal ceroid lipofuscinosis (NCL) involving a CLN6 variant

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Neuronal ceroid lipofuscinoses (NCLs) represent lysosomal storage disorders marked by seizures, motor difficulties, and vision loss. The underlying cause is associated with mutations in the ceroid lipofuscinosis (CLN) genes. The CLN6 protein, essential for lysosomal function, is an endoplasmic reticulum (ER) membrane protein featuring seven transmembrane domains. In this case report, we present the clinical details of a 7 years old girl with frequent seizures, speech regress, ataxia, unstable gait since she was 3 years old.. Brain MRI scans revealed high signal intensity in parietal lobes on T2-weighted images and cerebellar atrophy in fronto-temporal areas and cerebellum. An electroencephalogram (EEG) showed picture of encephalopathy, electrical status epilepticus in sleep. Employing next-generation sequencing on a epilepsy gene panel, we identified a pathogenic homozygous missense point mutation (c.407G A; p.R136H) in CLN6.The diagnosis of late infantile neuronal ceroid lipofuscinosis (NCL) and secondary epilepsy was established, leading to the prescription of different AEDs. However, at the 6-month follow-up, the epilepsy remained poorly controlled, and other symptoms showed no improvement. This marks the initial occurrence of NCL attributed to a CLN6 mutation, broadening the spectrum of genetic possibilities associated with NCLs. Typically, NCLs are not the primary consideration in cases like this. Employing a gene sequencing panel to explore instances of unexplained seizures and development delay proves beneficial in confirming the diagnosis.

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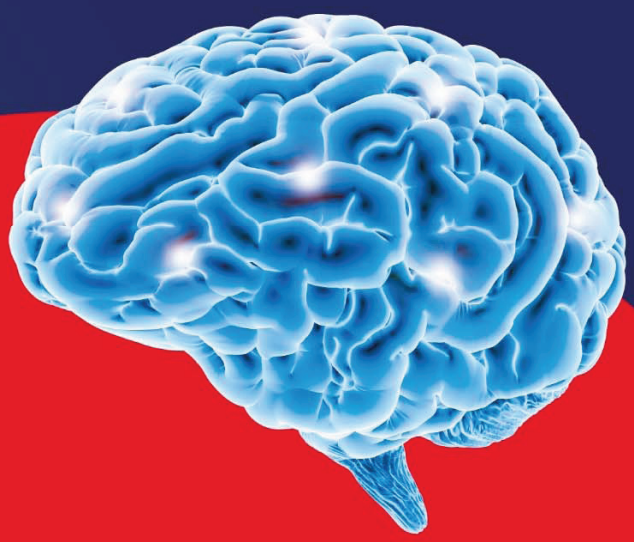
Headache



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Evaluation of rimegepant utilization patterns for acute and preventive treatment of migraine in a commercially insured population

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Objective: Assess the utilization and patient characteristics of rimegepant, an oral calcitonin gene-related peptide (CGRP) antagonist approved for migraine treatment and prevention in the United States.

Methods: This retrospective cohort study using US MarketScan administrative claims databases included patients ≥18 years old who newly initiated rimegepant with ≥1 refill between March 1, 2020 and January 31, 2023. Patients were divided into acute treatment (quantity=8 tablets) or prevention (quantity=15 or 16 tablets) cohorts, based on the index quantity dispensed, stratified by before and after the addition of the prevention indication (June 1, 2021). Utilization periods were defined as the time between the first and last prescription fills with an additional 90 days for 'as-needed' use. Patient characteristics and treatment history were assessed in the six months prior to index.

Results: Overall, 16,177 rimegepant users were identified. Among acute treatment users, tablet utilization (mean ± standard deviation) was 4.5 ± 2.2 tablets per 30 days over a follow-up period of 340 ± 187 days. Respective numbers among prevention users were 8.7 ± 2.8 tablets per 30 days and 225 ± 90 days. Rimegepant users (aged 43 ± 11.5 years; 88.4% were female) commonly used triptans (58.3%), non-steroidal anti-inflammatory drugs (35%), anti-CGRP monoclonal antibodies (30.5%), and opioids (30.3%) prior to initiation.

Conclusions: Tablet utilization for rimegepant acute treatment users was consistent over time and similar to literature benchmarks for migraine frequency. Lower than expected utilization in the assumed prevention users may be due to variable use patterns that requires further investigation.

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Predicting likelihood of idiopathic intracranial hypertension from imaging: A retrospective audit

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Objective: This retrospective audit was carried out with the aim of identifying if MRI features in patients suspected of Idiopathic intracranial hypertension (IIH) are statistically significantly associated with the diagnosis.

Methods: MRI images of all patients diagnosed with IIH according to modified Dandy criteria and an age and gender matched group of patients who had a diagnosis of migraine were re-reviewed by a neuroradiologist who was blinded to the final diagnosis and clinical history. We looked at 17 features in the MRI.

Results: When each of the MRI features were considered separately (univariate analysis), seven features were statistically significantly associated with IIH (p0.05). However, after adjusting for multiple comparisons and excluding collinearity, only optic nerve sheath distension (ONSD), peri-optic cerebrospinal fluid diameter and posterior globe flattening were associated with a diagnosis of IIH (Bonferroni adjusted p value 0.005).

Conclusion: While no individual feature could predict occurrence of IIH, Two or more MRI features. (ONSD / Peri-optic CSF diameter / posterior globe flattening, Right Meckel's curve AP diameter 11.5, Bright spot at fundus, Optic nerve tortuosity, Partial empty Sella) had a good sensitivity, specificity, positive and negative likelihood ratios. Radiologists' opinion regarding overall appearance was significant and this prediction was better for patients with high opening pressure. The imaging features identified in this study as being associated with IIH may be potentially useful to train an artificial intelligence-based algorithm to predict the likelihood of IIH from MRI, which in turn may be independent of the experience of the interpreter.

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Dual biological therapy in migraine with autoimmune rheumatic disease: is it plausible?

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Objectives: It is not clear whether migraine-type headache is a specific manifestation of an autoimmune disorder or a comorbidity which needs a better comprehension. Biological therapy is often indicated for both conditions separately, but data on dual therapy is still lacking.

Results: A 43 years old woman, was referred to a neurologist for severe migraine headaches. At the age of 24 she developed hands, hips pain and was diagnosed with HLA-B27 negative ankylosing spondylitis (AS). Due to high AS activity, the effect of NSAIDs and glucocorticosteroids became insufficient over the time. Biological therapy with adalimumab was added and later changed to etanercept. Rheumatological follow-up continued, the previous symptoms improved, but at the age of 41 migraine-type headaches became more frequent and intense, occured 16-17 days a month and lasted up to 72 hours. The patient indicated pronounced prodrome (fatigue) and accompanying symptoms (nausea, vomiting, photophobia). The neurological status was normal and brain MRI showed no significant changes. The condition met the criteria for migraine without aura and triptans were prescribed. As beta-blockers, NSAIDs were ineffective, biological therapy with fremanezumab 225 mg s/c per month was added. Headaches frequency reduced to 4 days a month, attacks became milder and the need for triptans decreased. Etanercept was also continued for AS.

Conclusions: Fremanezumab and etanercept was effective and well-tolerated. There is a lack of data on dual biological therapy in different pathologies. It still remains a controversy whether to prescribe biological drugs targeting various pathophysiological mechanisms and what combinations should be avoided.

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Migraine and disability from EHIS perspective

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Disability is the main feature of migraine related disease. Self-reported disability (SRD) can be useful tool for assessment disability. It represents the perception of patient's feeling and self-efficiency. The relationship with other socioeconomic, health related factors and other disease could be determined. Therefore, we explored the migraine's self-reported disability in Slovene population. The survey EHIS (European Health Interview Survey), conducted 2019, included 9900 adults, aged 15 years or older. Binary logistic regression was used in univariate as well as in multivariate analysis. Three multivariate models were defined - MODEL 1 consisted of stroke and comorbidities related to physical dimension of health, MODEL 2 consisted additionally of comorbidities related to mental dimension of health, while MODEL 3 consisted additionally of demographic and socioeconomic factors. In univariate analysis all included factors related to SRD. In multivariate analysis, MODEL 1, all included factor were significant and migraine related to SRD (p0.001). The strength of association did not change importantly. In MODEL 2 the factors of mental health additionally included into analysis. The relationship between migraine and SRD became insignificant (p=0,116) and strength of association importantly decrease. In the MODEL 3 which contained sociodemographic factors the association between migraine and SRD was low but significant (p=0.001).We have concluded migraine related to SRD in Slovenia. Disability associated with migraine could mostly be related to factors of mental dimension of health. Thus coping strategies should be directed toward prevention of mental comorbidies of migraine.

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Anticephalgic Mask

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A study was performed with 36 migraine patients. All patients applied a topical medication containing Rhus Toxicodendron and Bryonia in conjunction

with a photoprotective mask. 33 of the 36 patients stated that the treatment was extremely effective. On a 0-10 scale the average rating was 8.2. Furthermore, the average time to significant relief was approximately 20 minutes. There were no allergic reactions or significant side effects. The patients were able to cut down on opioids and other systemic migraine medications. Such a treatment is effective, quick, safe, and inexpensive. No rebound headaches were reported.

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Rare case of pediatric episodic migraine

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We report a 3,5-year-old boy , who was referred to our clinic by his primary care physician for evaluation of headache. He had normal birth/developmental history. His family had no remarkable medical history including headaches and dysautonomia. Parents reported that child had severe, sharp, pulsating headache since he was 2,5 years . No precipitating factor was detected such as head trauma, illness, asthma attack, and so on. These painful attacks were strictly left sided, lasting 48-72 minutes and located in the orbitofrontal and temporal regions, without any side shift. Frequency of pain attacks was once in a month during last year, had a sudden onset with a clear end, and were associated with left unilateral autonomic symptoms (conjunctival injection, lacrimation. Child becomes irritable, does not want to get out of bed, lies with his eyes closed, refuses to eat (photophobia, phonophobia), also fatigue, nausea, vomiting were present during headache. During the interictal period, he felt no pain and have normal daily activity. Neurological examination and blood tests was normal. Magnetic resonance imaging (MRI) did not show any brain abnormalities. EEG revealed no abnormalities. Taking into account the clinical manifestation, a diagnosis of episodic migraine mas made for the child. He was prescribed to take ibuprofen during headache attack and lifestyle modification. There is a significant risk of overlooking migraines in pediatric cases. Ensuring a proper diagnosis is crucial for preserving a high quality of life and preventing the use of inappropriate treatments.

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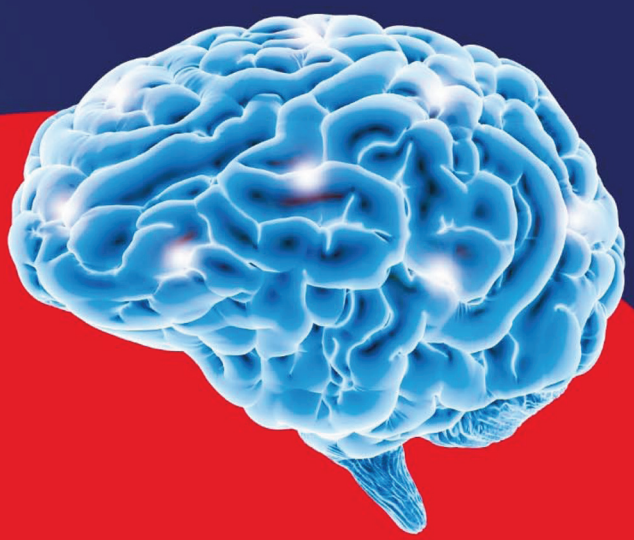
Multiple Sclerosis



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Controversies concerning the differential diagnosis between glioblastomas and pseudotumoral multiple sclerosis in young patients

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A glioblastoma in a patient diagnosed with multiple sclerosis (MS) represents an unusual clinical situation that can raise differential diagnosis issues. MS is not usually causing focal masses-like formations, but rather ovoid, homogeneous, small-sized, well-defined lesions without any mass effect. However, patients with multiple sclerosis can develop tumor-like growths in the so called tumefactive MS. Cerebral neoplasms can mimic, in the initial stages, MS manifestations.

Finally, there are extremely rare clinical situations in which a patient known to have MS can develop a secondary brain tumor: lymphoma, astrocytoma, oligodendroglioma, glioblastoma.

Further research needs to assess whether the rare association of the two conditions is coincidental or they may be triggered by common causal events. It is yet to be determined whether the evolution of the two coexisting ailments would have different evolutions compared to each being a singular pathology.

The frequency of brain tumors in patients with MS could be higher than in the general population, possibly due to the frequent MRI scans of these patients.

It is still unclear if the immunosuppressive treatment of MS might play a role in carcinogenesis, given that patients with MS have a lower risk of any type of cancer than the general population, except for an increased risk of brain and urinary tract malignancies.

We present the case of a female patient, known with MS, in whom, the appearance of newly rapidly evolving neurological symptoms required an imaging assessment. This revealed an expansive intracranial process. The brain biopsy established the diagnosis of glioblastoma.

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The role of SIRT1 and the possibility as a therapeutic target in multiple sclerosis

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Objective: The incidence rate of multiple sclerosis (MS) is increasing all over the world, which causes a great burden on society and the economy, and its mechanism is still unclear. To explore the role of silent information regulatory factor 1 (SIRT1) and the possibility as a therapeutic targets in MS.

Methods: SIRT1 is a type of NAD+dependent histone deacetylase widely present in different cells, which can participate in and regulate processes such as energy metabolism, oxidative stress, and inflammatory response in the body. It is an important molecular target for various traditional Chinese medicine monomers to exert disease protective effects and is involved in MS. Therefore, this article uses literature search methods to conduct relevant research on the pathogenesis and therapeutic targets of SIRT1 in MS.

Results: SIRT1 is highly expressed in the brain. When MS occurs, the SIRT1 protein plays an important role in its damage and neuroprotection. Research has shown that SIRT1 can exert anti-inflammatory, antioxidant stress, anti-apoptotic, and induced autophagy effects in MS. As a protective factor, SIRT1 exhibits a negative regulatory effect on various inflammatory cytokines and can alleviate experimental autoimmune encephalomyelitis. SIRT1 can be modified by adjusting AMPK/PGC1, SIRT1/HIF1α, SIRT1/PGC-1 α/ NLRP3 to reduce cell apoptosis, alleviate oxidative stress, and alleviate MS damage through inflammation.

Conclusion: SIRT1 may participate in MS by regulating oxidative stress, autophagy, apoptosis, inflammation, and other responses. Regulating SIRT1 expression may be a potential new therapeutic target for MS.

Keywords: Silent information regulatory factor 1; Multiple sclerosis; Immune mediation; Targeted regulation

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Phase 2 Efficacy and Safety of Frexalimab: 6-Month Results of a Novel CD40L Inhibitor in Relapsing Multiple Sclerosis

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Introduction: Frexalimab, a second-generation anti-CD40L monoclonal antibody blocks the CD40/CD40L costimulatory pathway that regulates adaptive and innate immune responses, without depleting lymphocytes. In the 12-week (W) double-blind-period of a phase 2 trial (NCT04879628), frexalimab$_{\text{high-dose}}$ demonstrated an 89% reduction (vs placebo) in new gadolinium-enhancing (Gd+) lesions in relapsing multiple sclerosis (MS) participants.

Aim: Present W24 efficacy and safety of frexalimab in the phase 2 open-label extension.

Methods: Participants aged 18-55 years were randomized to frexalimab$_{\text{high-dose}}$ (N=52), frexalimab$_{\text{low-dose}}$ (N=51), or matching placebo (placebo$_{\text{high-dose}}$: N=12, placebo$_{\text{low-dose}}$: N=14). At W12, participants receiving placebos switched to respective open-label frexalimab.

Results: 125/129 participants entered open-label-extension. The number of new Gd+ T1-lesions (unadjusted mean±SE) remained low in the frexalimab$_{\text{high-dose}}$ arm (W12, 0.2±0.08; W24, 0.1±0.05) and frexalimab$_{\text{low-dose}}$ arm (W12, 0.5±0.17; W24, 0.3±0.12). At W24, 96% of participants continuing frexalimab$_{\text{high-dose}}$ had no new Gd+ T1-lesions and 91% had no new/enlarging T2-lesions. In the frexalimab$_{\text{low-dose}}$ arm, 80% of participants continuing frexalimab$_{\text{low-dose}}$ had no new Gd+ T1-lesions and 74% had no new/enlarging T2-lesions at W24. In placebo-switch participants, new Gd+ T1-lesions decreased from 2.3±1.49 at W12 to 0.4±0.31 at W24 in the placebo$_{\text{high-dose}}$/frexalimab$_{\text{high-dose}}$ arm and 3.7±2.31 at W12 to 0.6±0.44 at W24 in the placebo$_{\text{low-dose}}$/frexalimab$_{\text{low-dose}}$ arm. Plasma NfL and CXCL13 levels decreased over W24 with frexalimab. There were no new safety concerns; the most common adverse events were COVID-19, nasopharyngitis and headache.

Conclusion: Frexalimab was well-tolerated and continued to show a pronounced reduction of new MRI lesions at W24. These findings support its development as a potential high-efficacy, non-lymphocyte-depleting, MS therapy.

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Is early-onset MS present with a more active course of the disease?

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Background: Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system, usually presenting at the age of 20 and 40 years. However, in rare cases, it is diagnosed before the age of 18 years, defined as early-onset MS (EOMS), or at the age of 50 years and later, described as late-onset MS (LOMS). Our goal was to determine the difference in disease activity among EOMS and LOMS patients.

Methods: We analyzed retrospective medical data of 88 patients, including 39,8% (35) EOMS and 60,2% (53) LOMS patients. The data included demographic, clinical, and radiological findings.

Results: The mean age at the time of the symptoms' onset in the EOMS group was 14.83 (SD=3.19) and 53.91 (SD=4.19) in the LOMS group. In EOMS group, RRMS disease course was the most common, while progressive MS was more frequent among LOMS group compared to EOMS group (p=0,001). The mean number of first year relapses in EOMS patients was higher (1,69, range 1-3) as compared to LOMS patients (0,68, range 0-2) (p0,001). Brain MRI repeated during the first year after diagnosis revealed new lesions in all EOMS patients, and in only 49,05% (26) of LOMS patients (p0,001). There was no significant difference in the frequency of active foci on MRI between the two groups (p=0,276).

Conclusion: The EOMS group had a more active disease course as there were more relapses in the first year, and signs of progressive disease were more often observed radiologically.

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A simple score (MOGR) to identify individuals at high risk of Relapse after MOGAD attack

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Background*:* Early recognition of markers of relapse in myelin-oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is key requisite of personalized attack prevention therapy and management for patients.

Objective*:* To identify early predictors of relapse in patients with MOGAD, derive and validate a simple risk score to predict relapse of MOGAD.

Methods*:* Using multi-center registry of China National Registry of Neuro-Inflammatory Diseases (CNRID, NCT05154370), identified patients with MOGAD in March 2023 and followed up prospectively in September 2023 for latest recurrence. Primary endpoint was MOGAD relapse. Included patients were randomly divided into model development (75%) and internal validation (25%) cohorts. AG models were used for prediction model construction and internal validation cohort were used to assess. Nomogram and relapse risk score were generated for the final prediction models.

Results*:* 188 patients (612 treatment episodes) were included in derivation and internal validation cohorts. female (HR: 0.687, 95% CI: 0.524-0.899, p = 0.006), onset Age ≥ 45 years old (HR: 1.621, 95% CI: 1.242-2.116, p 0.001), receive immunosuppressive therapy (HR: 0.338, 95% CI: 0.239-0.479, p 0.001), oral corticosteroids 3 months (HR 0.449, 95% CI 0.326-0.620, p 0.001) and onset phenotype (p 0.001) were associated with MOGAD relapse. A simple score [MOGR (Attack phenotype, Onset Age, Gender, Immunosuppressive therapy, oral Corticosteroids)] derived in prediction model was highly predictive of relapse of MOGAD. MOGR score of 13-16 indicates more higher risk of relapse (HR: 3.285, 95% CI: 1.473 - 7.327, p = 0.004).

Conclusion*:* The risk of MOGAD relapse seems to be predictable. MOGR score can be used in routine clinical practice helping clinicians to determine appropriate treatment.

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Patterns and Predictors of Multiple Sclerosis Phenotype Transitions Based on a Longitudinal Analysis Using the CLIMB Study

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Introduction: Multiple sclerosis (MS) characteristics vary over time, but little is known about transitions and predictors of change among phenotypes.

Objective: To investigate how people with multiple sclerosis (PwMS) transition between phenotypes, within the Comprehensive Longitudinal Investigation of MS at the Brigham and Women's Hospital (CLIMB) Study.

Methods: This retrospective analysis of US-based CLIMB Study identified PwMS (18-65 years [y]) diagnosed between 1/1/2000–31/12/2010, with ≥10y follow-up data. PwMS were categorized into relapsing-remitting MS (RRMS), primary-progressive MS (PPMS), and secondary-progressive MS (SPMS) (experiencing ≥1 relapses: active SPMS [aSPMS]; no relapses: nonrelapsing SPMS [nrSPMS] within 2y pre-index). Demographics were extracted alongside Expanded Disability Status Scale (EDSS) scores. Cox regression modelled time to MS diagnosis. Predictors of transition were determined by multivariate regression analyses.

Results: Among 565 people with RRMS, 95 (16.8%) transitioned to SPMS (median time-to-transition [range]: 10.4y [1.3-21.3y]) including 56 people with nrSPMS (58.9%) who never relapsed. Of the 39 pwMS with any aSPMS diagnosis, 32/39 (82.1%) transitioned to nrSPMS. The relative hazard to reach EDSS level 3, 4, or 6 were significantly lower for RRMS vs other phenotypes (all P0.0001). Older age at MS onset (HR [95% CI]: 1.05 [1.03-1.07]), and higher baseline EDSS (1.42 [1.26-1.62]) and DMT switches (1.21 [1.11-1.32]) were significant predictors of nrSPMS transition (all P0.001).

Conclusions: Among PwMS who transitioned from RRMS to SPMS, 41% overlapped with an active phenotype (aSPMS), while 59% transitioned without relapses (nrSPMS). Those transitioning through aSPMS were younger and more likely to have DMT escalation vs. those transitioning without relapse.

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Characteristics of People with Multiple Sclerosis by Phenotype Based on Cross-Sectional Analysis Using the CLIMB Study in the United States

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Introduction: Multiple sclerosis (MS) phenotypes are categorized based on its clinical course. Understanding how characteristics vary across phenotypes, and during transition is important, as treatment may impact long-term outcomes.

Objective: To investigate how MS prevalence and characteristics vary across phenotypes within the Comprehensive Longitudinal Investigation of MS at the Brigham and Women's Hospital (CLIMB) Study.

Methods: This retrospective analysis of the US-based CLIMB Study identified people with MS (PwMS) aged 18-65 years (y), stratified by relapsing-remitting MS (RRMS), primary-progressive MS (PPMS), active secondary-progressive MS (aSPMS),

and nonrelapsing secondary-progressive MS (nrSPMS) at "index" (22/12/2021). Demographics were extracted alongside Expanded Disability Status Scale (EDSS) scores. Data are presented as mean±SD.

Results: The study included 2,599 PwMS (RRMS: 1,891 [72.8%]; PPMS: 133 [5.1%]; nrSPMS: 534 [20.5%]; aSPMS: 41 [1.6%]) with 46.6%-75.9% females. Age at MS onset was lower for aSPMS (32.2±12.7y), RRMS (32.6±9.7y), and nrSPMS (33.8±10.4y) vs. PPMS (44.4±10.7y; P0.001). Age at transition was lower for aSPMS (45.4±10.7y) vs. nrSPMS (53.1±10.5y; P0.001). RRMS group had a shorter duration to first treatment vs. other phenotypes (4.2y vs. 7.2-9.4y; P0.001). At index, more people with RRMS (68.7%) and aSPMS (61.0%) received disease-modifying therapies (DMTs) vs. nrSPMS (58.2%) and PPMS (51.9%). EDSS scores were higher for nrSPMS (5.9±1.8), PPMS (5.9±1.8), and aSPMS (5.7±1.9) vs. RRMS (1.9±1.5; P0.001).

Conclusion: Among 2,599 PwMS, 20.5% had nrSPMS. nrSPMS and PPMS groups waited longer for first treatment and were less likely to receive DMTs, despite higher disability burden vs. RRMS, highlighting an unmet clinical need among people with progressive MS.

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Impact of Alemtuzumab on Fatigue, Quality of Life, and Patient/Caregiver Reported Outcomes in Relapsing-Remitting Multiple Sclerosis: Findings from a Real-World Evidence Study

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Background: Alemtuzumab is approved for treatment of highly active relapsing–remitting multiple sclerosis (RRMS) in the European Union. Patient reported outcomes (PROs) document information on the patients' disease state and assess the impact of alemtuzumab on their quality of life (QoL). Understanding the caregiver reported outcomes (CROs) in a real-life treatment setting is essential for MS treatment.

Methods: This 36-month, real-world, observational study enrolled 87 RRMS patients undergoing alemtuzumab treatment in three European countries. The primary endpoint was the effect on MS-related fatigue (Fatigue Scale for Motor and Cognitive Functions [FSMC]). Secondary endpoints included effect on cognition (Symbol Digit Modality Test [SDMT]), depression (Beck Depression Inventory–Version II

[BDI-II]), QoL (Multiple Sclerosis Impact Scale-29 item [MSIS-29]), treatment satisfaction, number of relapses, improvement in Expanded Disability Status Scale (EDSS) score, and safety. Exploratory endpoints included CROs.

Results: Of 87 enrolled patients, 72.4% (n=63) completed six follow-up visits. Statistically significant improvements were found for FSMC (p0.01), SDMT (p0.05), depression (p0.01) and QoL scores (MSIS-29, physical (p0.01) and psychological (p0.001)). Global treatment satisfaction (p0.001), effectiveness (p0.05) and side effects (p0.05; apart from at EOS) also showed significant improvements at all time points. The percentage of patients with at least one relapse remained consistent throughout the study (10.8%-13.2%). EDSS improved significantly (p0.05). Caregivers reported an increase in emotional QoL. One treatment-related death occurred, and no new safety concerns were reported.

Conclusion: This real-world study demonstrated beneficial impact of alemtuzumab on fatigue, cognition, depression, QoL and treatment satisfaction. Moreover, disability improvement over time was reported.

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"Multiple Sclerosis Hug": Challenging of a Peculiar Symptom

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Pain syndromes in Multiple Sclerosis are a challenging aspect. "Multiple sclerosis hug" is characterised by a tight, squeezing, or burning sensation around the chest or waist, similar to a constricting band or hug, and it may indicate a relapse.

A 46-year-old female, known with SPMS diagnosed at the age of 22, comes to our clinic with severe and persistent right-sided costal pain, exacerbated during inspiration, with an onset 3 months ago, and no response to conventional treatment.

No changes were observed in the neurological examination compared to the last clinical evaluation (EDSS = 5). The patient did not exhibit any truncal level of sensitivity. Blood tests, ultrasound, and cardiology exams did not reveal any acute pathological changes. The cerebral and spinal cord MRI did not show any new or active lesions. Research findings suggest that, despite the often-established link between relapses and MRI lesions, a substantial mismatch exists between clinical symptoms and the occurrence of MRI abnormalities.

After 5 days of taking 1g of methylprednisolone daily, complete pain relief was observed. Unfortunately, pain is not quantified in the functional sensitivity score, and in this case, despite a pain rating of 8 on the pain scale, this aspect does not increase the EDSS score.

Although it's not extensively documented in medical journals, this painful symptom could be useful for determining the course of action regarding treating a clinical relapse, escalating the use of disease-modifying therapies, and characterizing the disease course in MS.

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Safety and Effectiveness of Cladribine Tablets after Treatment with Natalizumab (CLADRINA) Trial – Interim Analysis

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Introduction: Natalizumab is a highly effective therapy approved for relapsing forms of multiple sclerosis (RMS) associated with an increased risk of developing progressive multifocal leukoencephalopathy (PML) and disease reactivation upon cessation. Cladribine tablets (CladT) are a highly effective therapy approved for RMS patients that preferentially reduces blood B and T lymphocytes.

Objectives: CLADRINA was designed to generate effectiveness and safety data regarding the transition of RMS patients from natalizumab to CladT.

Methods: CLADRINA is an open-label, phase 4, study in 40 RMS patients who switched to CladT within 4 weeks of their last natalizumab infusion.

Results: 39 patients completed 12 months of follow-up. In the 12 months prior to CladT switch, the mean annualized relapse rate (ARR) was 0.1 (95%CI:0.00-0.22) and decreased to 0.05 (95%CI:0.00-0.12) at 12 months. At baseline, the mean Expanded Disability Status Scale (EDSS) was 2.46 (range:0.0-5.5) and remained stable 12 months after switching to CladT. At baseline, 95% of patients were free from T1 gadolinium-enhancing (Gd+) lesions, and 12 months after switching, 100% were free from T1 Gd+ lesions. At baseline, 87.5% of patients were free from new/enlarging T2 lesions, and 12 months after switching, 97% of patients were free from new/enlarging T2 lesions. The therapy was well tolerated.

Conclusion: After switching to CladT from natalizumab, ARR, EDSS and MRI activity remained stable through 12 months. No cases of PML or rebound disease activity have been reported. Continuing to evaluate immunological and clinical data may provide further insight into advantages of this therapy transition.

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Balance control mechanism in people with multiple sclerosis using virtual reality environment

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Multiple Sclerosis (MS) is a progressive neurological condition characterized by deteriorating balance control, significantly increasing the risk of falls. As virtual reality (VR) emerges as a promising tool for balance training, this study investigates its effectiveness and impact on balance control mechanisms in MS patients, compared to healthy individuals. The primary objective is to explore balance control in MS patients within a VR environment and assess the efficacy of VR-based balance training. Employing an empirical approach, the study evaluates balance response in MS patients using VR technology. Data collection encompasses patient observations, along with physiological and biomechanical balance assessments. A preliminary systematic review and meta-analysis reveal variability in balance response assessments among MS patients. These assessments potentially offer crucial indicators of MS progression, aiding in personalized treatment and evaluating the effectiveness of interventions. Prior research suggests that MS patients practicing in VR environments acquire transferable balance skills applicable to real-world scenarios. The current study is expected to provide vital insights into the influence of VR on balance control among MS individuals. This research offers a comprehensive examination of balance acquisition in MS patients within VR settings. By integrating various physiological and biomechanical perspectives, it contributes to a deeper understanding of balance control mechanisms in MS. The study's empirical methodology delivers significant insights into balance in MS patients and the potential of VR in enhancing balance training effectiveness. The outcomes are anticipated to enrich our understanding of VR's impact on balance control mechanisms, thereby informing personalized intervention strategies in MS.

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Characteristics of Multiple Sclerosis in Urban and Rural Areas of Azerbaijan

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Introduction: Multiple sclerosis (MS) is an autoimmune, inflammatory disorder affecting the central nervous system, whose cause remains unknown and for which there is no comprehensive cure.

The aim of the study: This scientific work presents the results of a study conducted to investigate the characteristics of MS in patients, with a focus on their place of residence.

Materials and Methods: At the Neurological Center of the Ministry of Health of the Republic of Azerbaijan, located within the Republican Clinical Hospital named after Academician M.Mirgasimov, a special expert committee over a period of 10 years (01.01.2013-31.12.2022) examined and studied the medical records of 1796 patients diagnosed with MS or those whose diagnosis was reaffirmed.

Results and discussion: Probable first attacks in patients were more common at the age of 20-29 years, both in urban (41.3±1.4%) and rural (41.2±2.0%) areas. The average age at the time of the first relapses was 29.7±0.2 years (29.6±0.3 in urban areas and 29.7±0.3 in rural areas). According to the clinical course, relapsing MS was more frequent both in rural (80.3±1.6%) and urban areas (76.5±1.2%). The lethality rate among rural residents (2.8±0.7%) was higher than urban residents (2.2±0.4%), but the difference was not statistically significant (p=0.407).

Conclusion: The share of MS is higher in urban than rural areas, possible reason can be environmental factors and better access to medical services, including neurologists and radiologists (MRI exams), in cities. This leads to earlier diagnoses and shorter times between first attacks and diagnosis in urban populations compared to rural ones.

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MRI in multiple sclerosis follow-up: Does the BartsMS experience support the case for AI assistance?

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Introduction: The 2021 magnetic resonance imaging in MS (MAGNIMS) guidance offers benchmarks for MRI in people with multiple sclerosis (pwMS) on disease-modifying treatment (DMT). The MS service at Barts Health NHS Trust (BartsMS) has adopted an amended version of this guidance, with extended timelines following the COVID pandemic.

Aims: To review MRI monitoring of pwMS at BartsMS. To inform sample size in "AssistMS", a multicenter project testing artificial intelligence (AI) supported MRI reading in pwMS.

Methods: Demographics, timelines, reports and multi-disciplinary team (MDT) decisions were reviewed October-December 2022. Patients were identified via PACS.

Results: 189 pwMS undergoing MRI were identified. 160/189 datasets were obtained for DMT follow-up. Mean time from request to MRI 104 days (range 0-371); mean time since previous scan 595 days (9-2834); mean time for reporting 52 days (0-312). Of 25 pwMS discussed at MDT, mean time from acquisition to MDT was 84 days (11-331). MRI changes alone led to DMT changes in 9.5% (18/189).

Conclusion: Whilst MRI scans were obtained within recommended timelines, significant variation, and delays in reporting and MDT decisions, were observed. Backlogs due to shortage of neuroradiological expertise may be eased by employing AI-supported MRI registration and analysis.

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Maintaining efficacy, reinstating anti-JCV immunity in people with MS: The Natalizumab to Cladribine experience at Barts Health

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Background: Rapid elimination of Natalizumab and modest speed of onset of Cladribine might lead to the risk of re-emerging disease activity.

Aim: To evaluate the safety of switching from Natalizumab to Cladribine in our cohort of patients with MS.

Methods: Clinical audit of patients with MS who switched from Natalizumab to Cladribine between July 2019 and May 2023.

Results: Six patients were identified (5 men, and 1 woman). They were between 21 and 39 years old (median: 31.5 years). Median disease duration was 5 years (range: 3-11 years). Median EDSS when starting Cladribine was 1.75.

The reason for switching was the presence of JC virus serum antibodies with an index of 1.5 in five and patient preference in one.

Median Natalizumab infusions was 14 (range: 5-47). The mean switching interval was 4.8 weeks (range: 2-8). The latency period was due to completing vaccinations or prophylactic anti-TB treatment. The median follow-up period from the first day of taking Cladribine, was 29.5 months. None reported clinical relapse or worsening disability as assessed by EDSS. None had MRI activity, or signs of PML.

Conclusion: Switching from Natalizumab to Cladribine was safe and effective. We recommend a delay of no more than two weeks when switching.

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Coaching newly diagnosed people with multiple sclerosis

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Introduction: Rapid intervention to facilitate secondary prevention is key for people with multiple sclerosis (pwMS). However, the regular pathway for diagnosis and management in the UK lacks urgency, which may adversely impact on pwMS' adjustment to their new diagnosis and decision making. Evidence suggests that emotional support of pwMS during this early phase may be of particular importance for rapid disease modifying treatment (DMT) and beneficial lifestyle changes.

Aims: To report outcomes of a workshop focussing on sustainable coaching for newly diagnosed pwMS, including results of a pre- and post workshop questionnaire.

Methods: A two-day workshop, taking place in February 2024, will be led by a team experienced in coaching pwMS early after diagnosis. Modules will include (i) early interactions between healthcare professionals (HCPs) and pwMS, (ii) dealing with resistance, (iii) emotional care pathway development, (iv) goal setting, (v) role of quality of life trustees, and (vi) measuring success.

Results: Approximately 35 HCPs will participate in this first of its kind workshop, which will inform similar future training events.

Conclusion: The urgency with which pwMS should enter a holistic care setting, including early DMT, produces new challenges for HCPs and the NHS. Efficient coaching may enable pwMS to rapidly adapt to MS thereby minimising its detrimental effects on their quality of life.

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Exploring the Link Between Autonomic Dysregulation and Alexithymia in Patients with Multiple Sclerosis

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Introduction: Alexithymia, characterized by emotional blindness, is prevalent in numerous medical

conditions, including multiple sclerosis (MS). Autonomic dysregulation (AD) is observed in MS patients due to multifaceted causes. Despite the frequent occurrence of AD in MS, the interplay between alexithymia and AD remains unexplored.

Aim: This study aimed to assess the presence of AD and alexithymia in relapsing-remitting MS (RRMS) patients.

Methods: The prospective longitudinal study included 48 RRMS patients with a median age of 48,08 ± 7,77, and a median disease duration of 15,83 ± 5,59, assessed at baseline and six years later. The following clinical assessments were done: Back Depression Inventory (BDI), Composite Autonomic Symptom Scale 31 (COMPASS-31), Expanded Disability Status Scale (EDSS), and Toronto Alexithymia Scale 20 (TAS-20) which was performed only on the second assessment, since little evidence exists on the progression of alexithymia over time.

Results: Over a six-year study period, our cohort exhibited no significant changes in EDSS scores (p=0.069) and total AD score (p=0.866). Average BDI scores showed a decrease from the initial measurement (p=0.046). Positive correlations were identified between total AD score and TAS-20 (r=0,517, p0,001) scores, as well as between BDI scores and TAS20 scores (r=0,608, p0,001) on the second assessment.

Conclusion: High levels of alexithymia correlate with AD and depression in MS patients. According to the significant positive correlation between alexithymia with high scores on BDI, and COMPASS-31, we suggest that by admitting the potential negative impact of alexithymia in MS, screening for it is relevant for better management.

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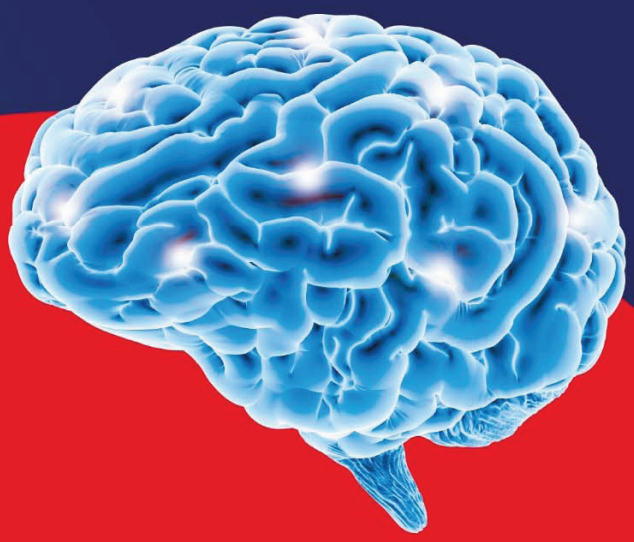

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A Case Report of Adult-Onset Leukoencephalopathy with Axonal Spheroids with Novel Mutation in CSFR1- Gene

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Introduction: Adult-Onset Leukoencephalopathy with Axonal Spheroids (ALSP) is a rare genetic disorder. To the best of our knowledge, there are no reported cases in Austria. We present a clinical case of suspected ALSP with regards to clinical, radiological and laboratory findings.

Case summary: A 50-year old female patient presentented with speech and concentration difficulties. Brain MRI showed bilateral confluent white matter lesions primarily in the frontal lobes with diffusion restriction in central parts, sparing subcortical U-fibers but involving the genu of the corpus callosum. Blood and cerebrospinal fluid examinations were negative for pleocytosis, oligoclonal bands, kappa free light chains, MOG- and aquaporin-4-antibodies. Further investigations including vasculitis parameters, ACE, homocysteine, tumor markers, vitamin B12 and infectious serology remained negative. CADASIL and CARASIL could not be confirmed by molecular genetics. Finally, a genetic examination for Hereditary Diffuse Leukoencephalopathy with Spheroids (HDLS) showed a c.2644_2646delCCA version on the CSF1R gene. Because of the limited data concerning pathogenicity of this variant, a clear connection from exclusively molecular genetic point of view could not be made in this case. Our patient experienced progressive deterioration in cognitive performance within 3 months. Neurological examinations revealed an increase in tone and increased reflexes.

Conclusion: Considering patient history, clinical and imaging findings as well as laboratory data including genetic tests, we suspect our patient of a rare genetic variant of ALSP with an underlying novel mutation.

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Fatigue, multidomain complaints, cognitive deficits and pattern of activation in severe COVID-19: behavioural and fMRI studies

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Introduction: Presence of mental fatigue and cognitive deficits in post-acute and early chronic stages of severe COVID-19 has been reported but few studies documented their occurrence in cases without prior or COVID-19-related brain damage. Aims of our studies are to determine how brain networks adapt during fMRI high-demand cognitive task and how the cognitive profile evolves in relation to the post-COVID-19 fatigue syndrome.

Methods: A fMRI pilot study has assessed in twenty-four normal subjects and in six consecutive patients with severe COVID-19 without brain damage, activation changes during a long colour-word Stroop task at 9 months. A behavioural pilot study has assessed in six consecutive patients with severe COVID-19 without brain damage, cognitive functioning, fatigue and multidomain complaints with a set of neuropsychological tests and questionnaires/scales at 12 months.

Results: Study 1: compared with controls, patients have presented different pattern of fatigue complaints, behavioural performance and/or activation networks, highlighting a trend towards two different effects: learning effect in controls and fatigue effect in patients. Study 2: a pervading mental fatigue and systematic multidomain complaints have been observed as well as association and dissociation between self-reported subjective mental fatigue, mental effort and cognitive performance.

Conclusion: In the chronic stage of severe COVID-19, even in the absence of brain damage, mental

fatigue/effort, multidomain/cognitive complaints and/or cognitive dysfunction tend to be observed. Neuronal recruitment during high-demand cognitive tasks tends to be partially re-organised, with interindividual variations. Impact of this re-organisation on long-term outcome and responsiveness to rehabilitation needs to be established.

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Electromagnetic stimulation regulates blood corticosterone levels in immobilized rats: gender differences

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Introduction. A mental disorder is a condition that affects an individual's cognition, emotional regulation, or behavior, causing distress or impairing main areas of functioning.

Methods. The effects of electromagnetic stimulation (EMS) and oxytocin (OXY) on blood corticosterone (CORT) levels in immobilized (10 days, 2 hours a day or one time, 2 hours) male and female rats while accounting for their sex hormone levels were studied. The experiments were conducted on intact and gonadectomized rats.

Results. As a result of immobilization, the content of CORT in the blood increased in both groups of rats. Chronic immobilization stress dysregulates HPA axis function in rats of both sexes. Gender differences are related to circulating gonadal hormones. Repeated EMS and OXY intranasal (IN OXY) (18 IU) (after each session of immobilization) or intracerebroventricular (1 μl/animal) returned the blood CORT level to normal. The effects of EMS and IN OXY were significant in intact rats compared with gonadectomized rats. Therefore, sex hormones play an essential role in maintaining the activity of the HPA axis and regulating negative feedback.

OXY released from the hypothalamus and adenohypophysis can inhibit CRF and ACTH secretion. Therefore, circulating OXY may inhibit CORT secretion directly from the adrenal glands (P0.01). Our results provide significant evidence to support the existence of a relationship between these two hormones.

Conclusion. EMS- and IN OXY -induced downregulation of corticosterone levels may improve stress-induced impairment of hypothalamic-pituitary-adrenal axis activity.

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Case report: A patient with Parkinson's disease and Syringomyelia or why every meeting with the patient should be like the first. S. Bozhinov, P. Bozhinov Neurology clinic, Heart and Brain Hospital, Pleven, Bulgaria

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Syringomyelia is a rare neurological disease associated with the formation of a cavity filled with cerebrospinal fluid within the spinal cord. The growth of this cavity gradually compresses various anatomical structures and leads to certain neurological symptoms. In the early stages of the disease, the clinical presentation can be concealed and misinterpreted as symptoms of other diseases.

We present a clinical case of a patient admited to the our neurology clinic with reduced muscle strength and atrophy of the muscles of the right hand, Parkinson's syndrome for the right limbs, and dissociated sensory loss in the lower cervical and upper thoracic segments. We performed an EMG study as well as MRI with contrast matter of the whole spinal cord and discovered an elongated high signal (on T2W) tubule-like lesion in the myelon with characteristics of Hydro/Syringomyelia. Due to the lack of therapeutic effect with levodopa and dopamine agonists in the past we performed a SPECT/CT with I123 DaTSCAN demonstrating bilateral dopaminergic degeneration in the striatum, more pronounced in the left one, corresponding to Parkinson's desease.

Conclusion: The presented clincial case demonstrates the importantance of conducting a detailed patient evaluation upon every clinical examination, including history, detailed neurological status, and advanced neuroimaging techniques, if appropriate, in order to make early diagnosis and discuss the following therapeutic options.

Key words: Syringomyelia, Parkinson's desease, MRI, Chiari malformation type 1.

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Electromagnetic stimulation improves chronic restraint stress-induced spatial memory impairment in rats of both sexes

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Introduction. Electric magnetic stimulation (EMS) is a noninvasive treatment method that is used in many neurodegenerative diseases. The study aimed to investigate the correlates of cognitive function in the chronic restraint stress model of rats of both sexes on the background of EMS.

Methods. Experiments were conducted on intact and gonadectomized rats both gender (n=32, 4–6 months old, 190- 220 g). Parameters of EMS were detected in experiments. Chronic restraint stress (CRS) performed 2 hours, during 10 days. The process of learning was studied using an elevated multibranch maze. The learning ability was tested 7, 14, and 30 days after the learning test. Data reliability was assessed using ANOVA.

Results. After immobilization, the learning ability was impaired in rats of both sexes ($P \leq 0.01$) compared to unstressed rats. Stressed rats did not remember the correct trajectory of the maze ($P \leq 0.01$). The number of mistakes was higher than in unstressed rats. The immobilized rats could not complete the task even on the 5th day of the train. The EMS improves learning time only in intact stressed rats. In gonadectomized rats, the EMS had minimal effects. EMS might affect the imbalances of neurotransmitter systems and hyperactivity of the HPA axis, which are essentially responsible for the expression of depressive-like behavior and fear responses only in the presence of sex hormones.

Conclusion. EMS has an anxiolytic effect in immobilized rats. This treatment improves learning and retention of information in stressed rats of both sexes. The research supported by the Shota Rustaveli National Science Foundation N FR-22-13-19

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Adverse childhood experiences impair spatial memory in adulthood

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Introduction. Adverse Childhood Experiences (ACE) in adulthood are associated with neurodegenerative diseases and impairment of cognitive function. ACE causes hippocampal neurodevelopmental dysfunction and alters hypothalamic-pituitary-adrenal (HPA) axis activity, although there is still no complete understanding of these effects.

Methods. For the formation of moderate stress in the early postnatal (PN) age, the Chronic Immobilization Stress (CIS) model (immobilization from PN0 to PN20 for 2 hours for 20 days) was chosen. The impact of CIS on cognitive function and behavioral manifestations in adult female rats was studied. To determine the possible therapeutic effects of electric magnetic stimulation (EMS), stressed rats received EMS additionally. In this group of rats, the behavioral and cognitive functions in adulthood (PN80) were established. Data reliability was assessed by ANOVA.

Results. ACE has been shown to cause cognitive impairment in adulthood. Stressed adolescents took longer to complete the correct trajectory in the elevated maze test. They made more errors than unstressed rats. EMS improved the time pass in the maze ($P \leq 0.01$). These data were similar to those of non-stressed female rats. The EMS had positive effects on hippocampal-dependent memory (elevated maze test) in stressed rats depending on sex hormone levels. Also, EMS enhanced the negative feedback of glucocorticoids on glucocorticoid receptors in adult rats.

Conclusion: EMS is a non-invasive treatment method that might be used as a complementary drug for the treatment of different neurodegenerative diseases caused by ACE.

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FOG score is an effective tool to assess freezing of gait in Parkinson's disease patients

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Background: Freezing of gait (FOG) is an episodic phenomenon, which limits mobility in advanced Parkinson's disease (PD). FOG can be overlooked during routine examination and may not always respond to treatment, including levodopa and deep brain stimulation (DBS).OBJECTIVE: To evaluate the most suitable clinical test to detect FOG in PD patients treated with DBS.

Patients and Methods: FOG was assessed in 32 PD patients (5 F, 27 M, average age of 59.9±6.5 years), treated with dopaminergic medication and DBS (lasting 4.9±3.3 years). Patients filled Freezing of Gait Questionnaire (FOGQ) as a screening tool and underwent tests of gait: Timed Up and Go test (TUG), 10m Speed walk test (SWT), Short step test (SST) and FOG score according to Ziegler.

Results: Twenty-seven patients reported FOG in FOGQ. FOG score revealed FOG in 22 patients (total score 8.3±SD 9.7), TUG in 10, SST in 8 and SWT in 2. The total FOG score showed significant correlation with FOGQ (r=0.50, p=0.003), even higher in single task subscore (r = 0.56, p 0.001) and dual motor task (r = 0.65, p 0.001). Two patients with negative screening performed FOG in SST and FOG score – dual motor/mental task.

Conclusion: Majority (84%) of our patients with advanced-stage Parkinson's disease on DBS therapy referred FOG according to FOGQ. The Ziegler test seems to be the most sensitive clinical tool, single motor and dual motor tasks show good correlation with referred FOG, dual motor/mental task can reveal FOG even in patients with negative screening.

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Transcranial Sonography Characteristics Of Cerebellar Neurodegenerative Ataxias

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Introduction: Cerebellar neurodegenerative ataxias encompass disorders affecting the cerebellum and its pathways. Transcranial sonography (TCS) has been used for the evaluation of brain parenchymal structures in various diseases especially in neuropsychiatric and neurodegenerative diseases. The aim was to investigate TCS characteristics of patients with neurodegenerative cerebellar ataxias.

Materials and methods: We included a total of 74 patients with cerebellar degenerative ataxia, 36.5 had autosomal dominant, while 33.8% had sporadic onset. Standardised ultrasonographic planes were used for the identification of brain structures of interest. All patients were clinically evaluated using SARA, INAS, neuropsychological and psychiatric scales.

Results: The brainstem raphe was discontinued in 33.8% of patients. The substantia nigra (SN) hyperechogenicity was identified in 79.7%. Third and fourth ventricle enlargement had 79.7% and 45.9% of patients, respectively. A positive and statistically significant correlation was found between SN hyperechogenicity with dystonia (p0.01), rigidity and dyskinesia (p0.05). Higher SARA total score statistically significantly correlated with the larger diameter of III (r=0.373; p=0.001) and IV ventricle (r=0.324; p=0.005). In such patients echogenicity of substantia nigra has been linked to extrapyramidal signs and raphe discontinuity to depression. Furthermore, ataxia and its clinical subtypes have positively correlated with IV ventricle diameter indicating brain atrophy and brain mass reduction.

Conclusion: In our study we have shown the main TCS characteristics of patients with neurodegenerative ataxias. Our results have shown that TCS is an effective, dependent and reproducible technique in monitoring patients with neurodegenerative ataxias.

Keywords: neurodegenerative cerebellar ataxias; transcranial sonography; hyperechogenicity, ventricle enlargement, raphe discontinuity

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Autoimmune Involvement in CANVAS: Exploring the Association with Vitiligo and Implications for Ganglionopathy and Vestibular Failure. A Case Report and Literature Review

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Objective: To report a case of CANVAS with vitiligo and its autoimmune implications for ganglionopathy and vestibular failure.

Background: CANVAS, a recently described neurological syndrome, presents as adult-onset ataxia with potential inheritance patterns of autosomal dominant or recessive origin. However, the precise pathophysiological mechanism underlying CANVAS remains elusive. Particularly, speculation has arisen regarding a possible autoimmune component in its etiology.

Methodology/Design: Case Report and Literature Review.

Results/Case Presentation: A 51-year-old woman came for incoordination. Previous MRI revealed cerebellar atrophy and electrodiagnostic studies were consistent with sensory axonal polyneuropathy. There was no chronic exposure to alcohol, heavy metals/toxins, and a negative FHx of neuropathy. The exam revealed vitiligo in her upper extremities, variable portions of her face, and lower extremities, and no organomegaly. There was hypotonia in all extremities, normal muscle power, and absent knee and ankle reflexes. There was limb ataxia on finger-to-nose testing, and rapid alternating movements were slowed. Gait was broad-based and ataxic, with swaying and incoordination. Sensory examination showed intact light touch and positional sense. Vestibular testing showed a marked reduction of the VOR function in horizontal canals consistent with vestibular areflexia. Routine blood work, including Sjogren's, heavy metals, serum B12/folate, thyroid function testing, and genetics all were negative.

Conclusion: While vitiligo is not part of CANVAS diagnostic criteria, there's an emerging association between autoimmunity and CANVAS. Genetic factors are implicated in some cases. The presence of autoimmunity (vitiligo) in a CANVAS-like presentation suggests a potential autoimmune mechanism, urging further investigation for this subset of patients.

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Time perception in Alzheimer's disease and Parkinson's disease

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Time perception is one of the most important functions of the brain, necessary for a person in everyday life for independent functioning, which undergoes significant pathological changes in patients with neurodegenerative diseases.

We aimed to investigate time perception in patients with Alzheimer's disease (AD) and Parkinson's disease (PD).

We examined 20 patients with PD (10 right-onset and 10 left-onset) and 15 patients with AD. All the patients underwent examination on MoCA, MMSE, The Apathy Scale, Plutchik's Impulsivity Scale. We conducted tests for implicit and explicit time perception. Implicit time perception tests included video test where patient should determine the duration of symbol appearance and question after 20 minutes of entering room how long time passed from the beginning to now. The explicit test was performed with a stopwatch indicating intervals of 5 seconds 4 times. Parkinsonism severity in patients with PD was assessed with UPDRS-III.

In AD, implicit time perception was more impaired, in both test of 20 minutes and video-test. It was associated with cognitive impairment (p0,05), time was lost in memory. In PD, there was a tendency toward changes in both implicit and explicit time perception, in the absence of other cognitive impairments, impulsive disorders, and regardless of the severity of motor disturbances. Patients with right-onset had more impaired time perception compared to left-onset patients (p0,05).

Our findings suggest time perception disturbances in patients with both PD and AD. Further continuation and expansion of this research will allow us to detail the characteristics and pathoanatomy of these changes.

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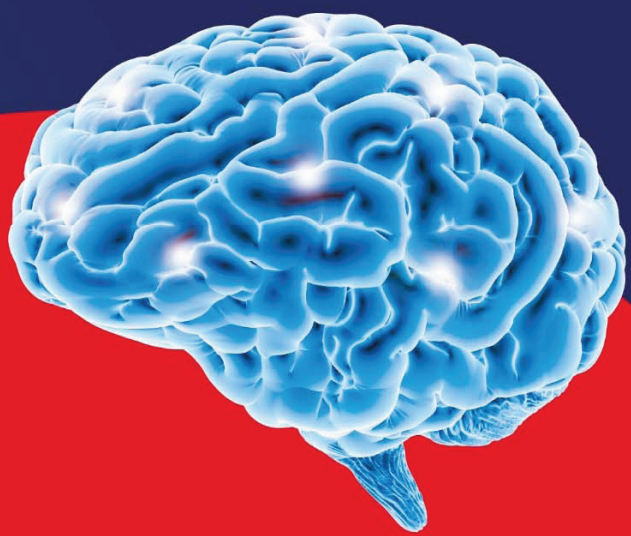

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Unusual Neurological Complications of Immune Checkpoint Inhibitors used in Treatment of Cancer: Report of two cases

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Introduction: Immune checkpoints are necessary molecules that either promote or inhinbit T-cell activation. Checkpoint inhibitors (ICI) that block these checkpoints allows T-cell to kill cancer cells. Neurological complications secondary to these novel cancer therapy are very rare and we report two such cases.

Methods: Retrospective case series study.

Results: Case (1) 78 years old woman who presented with subacute onset of dysarthria and cerebellar ataxia with previously treated high grade urothelial cancer with Nivolumab. Her MRI, CSF, routine blood work and paraneoplastic panels were all negative. She responded partially with high dose steroids and 4 courses of IVIG but still requires ongoing attendent's care.

Case (2) 70 years old man with subacute onset of dizziness, ataxia, orthostatic hypotension and autonomic dysfunction with previously treated bladder cancer with Pembrolizumab. His MRI shows enhancement in area postrema and (+) CSF anti-GAD65 antibody. He responded partially to high dose steroids, IVIG and plasma exchange. He continues to remain symptomatic with dizziness but his autonomic and area postrema symptoms had improved.

Conclusions: Serious but very rare, and delayed Neurological complications such as subacute cerebellar syndrome or autoimmune encephalitis due to ICI therapy for cancer should be suspected in those patients whose clincial presentation cannot be explained by other etiologies.

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Efficacy and Safety of Inebilizumab in Patients 50 years of age and older with Neuromyelitis Optica Spectrum Disorder: N-MOmentum Study Subgroup Analysis

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Background: Inebilizumab (INEB), an anti-CD19 B cell depleting antibody, is approved for the treatment of NMOSD in adults seropositive for aquaporin-4 antibody (AQP4-IgG+). The N-MOmentum study included participants with ages ranging from 18 to 74 years (yrs).

Objective: To evaluate the efficacy and safety of INEB in AQP4-IgG+ participants ≥50 yrs with NMOSD.

Methods: N-MOmentum (NCT02200770), a double-blind, phase 2/3 trial, assessed the efficacy and safety of INEB in adults with NMOSD, with a 28-

week randomized controlled period (RCP) (INEB 300 mg or placebo [PBO] on days 1 and 15), and an open-label period (OLP) of ≥2 years. Post hoc analyses were conducted to analyze outcomes in AQP4-IgG+ participants ≥50 yrs.

Results: Of 213 AQP4-IgG+ participants, 65(30.5%) were ≥50 and 148(69.5%) were

Conclusion: This data supports the efficacy and safety of INEB in AQP4-IgG+ ≥50 yrs NMOSD although evaluation of larger populations is needed to confirm these results.

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Progressive Multifocal Leukoencephalopathy and Subacute Sclerosing Panencephalitis: Viruses, Antigens and Antibodies

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Progressive multifocal leukoencephalopathy (PML) is a rapidly progressive demyelinating infectious disease of the central nervous system with asymmetric brain damage. Caused by activation of human polyomavirus 2, which is carried by about 80 per cent of the US population. Human polyomavirus 2 or JC virus is one of six species of human polyomaviruses and was named after the initials of the patient John Cunningham, in whom it was first discovered in 1971. Its activation in the human body is preceded by significant suppression of the immune system: in the vast majority of cases, PML is a manifestation of acquired immunodeficiency syndrome (AIDS), in other cases, after immunosuppressive and immunomodulatory therapy, for example, as part of treatment with monoclonal antibodies or after organ transplantation, as well as hematological neoplasms, such as Hodgkin's disease, chronic lymphocytic leukemia. Disease is especially common after bone marrow transplantation. Problem is the occurrence of PML in patients with multiple sclerosis treated with natalizumab.

Subacute sclerosing panencephalitis (SSPE) is a progressive neurodegenerative, most often fatal disease of the central nervous system caused by the measles virus. The disease is a slow viral infection; after the initial measles infection, there is an asymptomatic period that lasts an average of 7 years, but can vary from 1 month to 27 years.

It is estimated that on average 2 in 10,000 people who have measles develop it, with immunization being the main factor in the decline. In classic picture of the disease, death occurs between 1 and 3 years

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Acquired idiopathic generalized anhidrosis after COVID-19 infection

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Background: Acquired idiopathic generalized anhidrosis (AIGA) is an infrequent condition characterized by the sudden onset of an inability to sweat without accompanying neurologic features or sweat gland abnormalities, often leading to heatstroke. Several reports have postulated various pathogenesis about autoimmune responses in AIGA patients. The novel coronavirus (SARS-CoV-2) has been implicated in inducing autoimmune disease, prompting consideration of its potential role in the development of de novo autoimmune diseases.

Case: We present a case of a 34-year-old male with 16-week history of decreased sweating. Two weeks after a confirmed SARS-CoV-2 infection, he experienced facial flushing. subsequently, with increasing ambient temperature, the patient developed tingling in the palm, and urticaria in response to exercise with an absence of overall body perspiration. Quantitative sudomotor axon reflex test by Q-Sweat revealed absent sweat output at all sites. Laboratory studies for autoimmune diseases were normal. A skin biopsy from the palm revealed mild lymphocytic infiltration around the secretary portion of eccrine gland. Intravenously administration of methylprednisolone (1000 mg/day for five consecutive days) resulted in significant improvement of anhidrosis within several days.

Discussion: The hyperstimulation of the host immune system induced by SARS-CoV-2 infection and its vaccination has been linked to the development of autoimmune diseases. While the casual relationship between COVID-19 vaccination or infection and

AIGA remains speculative, Nonetheless, the short incubation period and positive response to steroid in our case suggest a potential autoimmune association between AIGA and SARS-CoV-2 infection.

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Cerebral Cortical Encephalitis in a child with MOGAD and Hashimoto's Thyroiditis

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Cerebral Cortical Encephalitis (CCE) is a rare phenomenon of Myelin Oligocyte glycoprotein-associated disease (MOGAD). Having concurrent anti-thyroid antibodies has not been reported. The characteristic feature of CCE is its involvement of the cerebral cortex which is appreciated in the FLAIR images of MRI. CCE patients usually present with cortical signs. We hereby, describe a case of CCE in a Bangladeshi child who presented with a 3-week history of progressive behavioral abnormalities, bilateral visual impairment, and hemiparesis following an attack of seizure. Examination poor visual acuity (OD to finger counting and OS to light perception) with funduscopic evidence of bilateral papilledema, and right arm and leg weakness. MRI showed predominantly cortical but also subcortical hyperintense lesions with subtle contrast enhancement. Further investigations elicited positive anti-MOG IgG antibodies in the serum concomitantly with high titer of anti-TPO Antibody, high TSH, and low FT4. Coexistence of CCE phenotype of MOGAD with Hashimoto's Thyroiditis is a rare occurrence. Treatment with corticosteroids and Levothyroxine reversed the clinical manifestations within a few weeks. However, at 6 months follow up while on a low maintenance dose of Prednisolone and levothyroxine, serum anti-MOG IgG was still detected to be positive along with positive Anti TPO and TG antibodies despite complete recovery of symptoms. This finding persuaded us to continue oral steroid therapy for a longer duration. This case underscores the need to look for other associated antibodies in MOGAD as failure to do so may impact the outcome and monitoring the disappearance of the antibodies.

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Long-Term Comparative Efficacy of Inebilizumab in the AQP4+ Subpopulation from N-MOmentum Open-Label Period Versus Azathioprine and Immunosuppressants and Versus Placebo in Patients with NMOSD

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Background: Inebilizumab (INEB), an anti-CD19 B cell-depleting antibody, is approved for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adults seropositive for aquaporin-4 antibody (AQP4+). N-MOmentum (NCT02200770) consisted of a 28-week randomized-controlled-period (RCP) and an optional open-label-period (OLP, 2 years) in which all participants received treatment with INEB.

Objective: To evaluate the long-term comparative efficacy of INEB over N-MOmentum OLP vs azathioprine and other immunosuppressants (AZA/IST) and vs historical-placebo (PBO) in participants with NMOSD.

Methods: Two historical comparator groups (HCGs) of participants who received AZA/IST (N=132) or

PBO only (N=106) were derived using data from published NMOSD studies and were used to evaluate the comparative efficacy of INEB (N=208) over the OLP. Hazard ratios (HR) for INEB vs HCGs were estimated using a Cox proportional hazards (PH) regression. Time to NMOSD attack was analyzed using parametric and flexible survival (spline) models that were fit to INEB and HCGs.

Results: The HR (95% CI) of time to NMOSD attack for the N-MOmentum PBO group compared to historical-PBO groups was 1.15 (0.67–1.91); P=0.58. The HR (95% CI) for time to NMOSD attack for INEB vs AZA/IST and PBO groups were 0.29 (0.17,0.42); P

Conclusions: INEB was associated with a statistically significant improvement in time to onset of an NMOSD attack and provided a long-term attack-free survival benefit over the OLP compared to the relative short-term benefit observed with AZA/IST.

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The relationship between autophagy and LCN2 secretion by reactive astrocytes

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Objective: Autophagy is a conservative lysosome degradation pathway, that can degrade and recover long-lived or misfolded protein and damaged organelles to maintain cell energy and function. LCN2 secreted by reactive astrocytes can induce the death of damaged neurons. Under inflammatory conditions, astrocytes secrete lipid delivery protein-2 (LCN2), which has recently been discussed as a valuable biomarker for predicting the clinical outcome of stroke patients. To summarize the relationship between autophagy and LCN2 and to explore whether autophagy can reduce the secretion of LCN2 by reactive astrocytes induced by OGD/R, which may be beneficial to neuroprotection.

Methods: Through the databases of China Knowledge Network, PubMed, Wanfang, etc., we searched “autophagy”, “LCN2” and “astrocytes” as keywords, collected related literature, and reviewed this problem.

Results: Deferriamine improved the up-regulation of Lipocalin-2 induced by lipopolysaccharide through autophagy activation of primary astrocytes. Torin-1 can inhibit the activation of autophagy flux in non-reactive and LPS-induced reactive astrocytes by MTOR, resulting in faster degradation of LCN2, intracellular LCN2 can be degraded by autophagy lysosome pathway, and the activation of autophagy flux accelerates its degradation before secretion. However, some reports suggest that LCN2 can reduce autophagy flux, and the increase of LCN2 in RPE reduces autophagy and activates the process of inflammatory body-iron apoptosis in dry AMD mice. Conclusion: Regulating the autophagy of astrocytes to affect the secretion of LCN2 may be a new strategy in treating central nervous system diseases in the future.

Key words: astrocytes; autophagy; LCN2; ischemic stroke

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Hydroxy-safflower Yellow A Inhibited NLRP3 Expression In Microglia After Ischemic Stroke Through TLR4/NF-κB Signaling Pathway To Reduce Neuroinflammatory Injury

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Objective: NLRP3 expression in microglia after cerebral ischemia and hypoxia (CIH) increases brain injury, but its specific mechanism is not clear. Hydroxysafflower Yellow A (HSYA) has anti-ischemia and anti-inflammatory effects. However, whether it affects the expression of NLRP3 in microglia cells after CIH and its mechanism remains unclear. To investigate the effect of HSYA on NLRP3 expression in microglia after cerebral ischemia injury and its mechanism.

Methods: The model of middle cerebral artery occlusion and reperfusion (MCAO/R) was established in male SD rats. BV2 was used to establish a glucose-oxygen-deprivation model in vitro. TTC staining, Western blot, immunofluorescence and ELISA were used to detect the relevant parameters.

Results: Compared with the sham operation group, cerebral infarction volume in the MCAO/R group was significantly increased, and was reduced and nerve function improved after HSYA treatment. The expressions of TLR4, NF-**κ**B and NLRP3 in the MCAO/R group were higher than those in sham group, and decreased after HSYA treatment. The levels of IL-1β and TNF-α in the MCAO/R group were higher than those in sham operation group, and HSYA inhibited the expressions. The expressions of TLR4, NF-κB and NLRP3 in the deoxygenated reoxygenated group were significantly higher than those in the control group, and were inhibited after the addition of HSYA.

Conclusion: HSYA may inhibit NLRP3 expression in microglia after CIH by regulating TLR4/NF-κB signaling pathways, thereby alleviating brain injury.
Keywords: Hydroxy-safflower Yellow A; NLRP3; Ischemic stroke; TLR4/NF-κB signaling pathway

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Unveiling the Link: Hyponatremia as a Precursor to Guillain-Barré Syndrome Onset

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Guillain–Barré Syndrome (GBS) is an inflammatory polyradiculoneuropathy which is known to produce syndrome of inappropriate Secretion of Antidiuretic Hormone (SIADH). In this report, we describe a rare presentation of GBS in a 64-year-old female, where hyponatremia preceded the typical muscle weakness, following a febrile illness a month prior, came to the emergency department with acute weakness and numbness. Remarkably, severe hyponatremia (116 mmol/L) was observed before the onset of GBS symptoms. Neurological examination revealed quadriparesis and sensory neuropathy with a distinct "glove and stocking" distribution. Extensive diagnostic investigations, including imaging and CSF analysis, ruled out alternative pathologies. The patient had a history of hospitalization for hyponatremia ten days before, and despite plasmapheresis and interventions for hyponatremia, no immediate improvement occurred. Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) was identified as the primary cause of hyponatremia, and a therapeutic regimen, involving Tolvaptan and fluid restriction, led to a gradual resolution of hyponatremia over two weeks. Notable neurological improvement was observed upon a follow-up, emphasizing the importance of a comprehensive diagnostic approach in cases where unexplained SIADH precedes GBS, especially in the context of antecedent febrile illness. This rare presentation underscores the need for nuanced evaluation for timely identification and management of GBS.

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A case of suspected tumor-like demyelinating disease with spinal cord involvement

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Background: Tumor-like inflammatory demyelinating disease (TIDD) is a rare primary demyelinating disorder of the central nervous system, also referred to as "demyelinating pseudotumor", because of its magnetic resonance imaging (MRI) appearance. Because it manifests with focal lesions of demyelination larger than 2 cm with a mass effect, it can easily be mistaken, both clinically and radiologically, for brain malignancies, such as gliomas. Although TIDD primarily affects the brain, isolated spinal cord involvement occurs in a small number of instances.

Case presentation: We present a rare case of a 35-year-old man who experienced cervical spine pain, a distal sensory deficit that gradually affected the abdomen and thoracic areas, and urine incontinence. The initial blood samples, CSF analysis, serological and microbiological tests were negative. MRI of cervical and thoracic spine revealed two hyperintense lesions in the spinal cord on T2 - weighted images at C3-C4 and Th11 levels with a slight mass effect. Antibodies against aquaporin-4 and myelin-oligodendrocyte glycoprotein (MOG) were tested further and found to be within normal limits. Based on the neuroradiological criteria, demyelinating process and spinal cord malignancy were included in the differential diagnosis. A high-dose corticosteroid treatment was administered, with a slight clinical improvement. A follow-up MRI after one month revealed a reduction of spinal cord lesions.

Conclusion: A combination of clinical presentation, MRI features, and surgical biopsy is typically used to diagnose localized tumor-like demyelinating lesions. Given the fact that demyelinating processe are usually caused by autoimmune mechanisms, corticosteroid therapy may be beneficial under particular circumstances.

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Epidemiological, clinical and radiological spectrum of connective tissue disease related neurological disorders — an ambispective observational study

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Background: Neurological manifestations are recognized increasingly in patients with connective tissue disorders (CTD) and account for a considerable proportion of morbidity and mortality associated with this disease. A**i**m – To study the epidemiological, clinical-radiological features of connective tissue disease having neurological manifestations and impact of neurological manifestation on Quality Of life of CTD patients.

Materials and Methods: An ambispective study was carried out at a tertiary care center where 66 patients of CTD with neurological manifestations were recruited. Quality of life was assessed with Euro QOL 5D questionnaire.

Results: We recruited 66 patients of CTD having neurological manifestations. In 40 patients(60.6%), neurological manifestation were the presenting feature. Out of 66 patients, 17(25.8%) were of SLE, 14(21.2%) of primary Sjogren syndrome and 10 (15.2%) were of systemic sclerosis. The commonest neurological features were PNS manifestations, found in 35 patients(53%) ,followed by CNS manifestations in 34 patients(51.5%) and psychiatry manifestations in 11 patients(16.7%). CNS manifestation included headache in 30 patients(45.45%), seizure disorder in 12 (18.2%), myelopathy in 10 patients(15.2%) and CNS demyelination in 9 patients(13.6%). PNS manifestations were myopathy in 25 (37.9%) patients, followed by polyneuropathy in 10 (15.2%) patients. Most common psychiatry manifestations were Anxiety disorder 11 (16.7%) followed by mood disorder 10(15.2%). Quality of life measured by EURO-QOL 5D score were severely impaired in patients of APLA, Neuro-Behcet and MCTD.

Conclusion: As CTD is an uncommon disorder, this study is important to understand the various neurological manifestations associated with it in Indian population.

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Monitoring the intensity of oxidative stress, apoptosis and inflammation in rat brain during lipopolysaccharide-induced endotoxemia: modulatory effect of melatonin

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Introduction: Lipopolysaccharide(LPS) is an integral part of the cell walls of gram-negative bacteria, so it causes damage to many organs (brain, liver, heart). Lipopolysaccharide-induced endotoxemia leads to overproduction of proinflammatory cytokines and reactive oxygen species in brain tissue. Melatonin(MLT) is a neurohormone that is synthesized from tryptophan and exhibits antioxidant effect.

The Aim: The objective of this research was to evaluate the effect of melatonin in the prevention of brain damage caused by Escherichia coli lipopolysaccharide, by analyzing: the level of oxidative stress (by monitoring malondialdehyde-MDA and carbonyl groups-PCC), apoptosis (DNase I and Caspase-3 activity) and parameters inflammation (NF-kB, IL-6 and TNF-), as well as the effects of melatonin supplementation on the investigated parameters.

Material and Methods: Twenty-eight Wistar Albino rats were randomly divided into four groups (n=7) as follows: Control group, MLT group(50 mg/kg), LPS group(10 mg/kg) and LPS+MLT group.

Results: In the brains of rats treated with LPS, the concentrations of MDA and PCC, as well as the activities of DNase I and Caspase-3 were significantly increased(p0.001), while the administration of MLT led to a decrease in the level of these parameters(p0.01). Application of melatonin to animals with endotoxemia(LPS+MLT group) significantly normalized the high levels of NF-kB, IL-6 and TNF-α in the brain tissue, compared to the LPS group(p0.05).

Conclusion: This study showed a significant therapeutic effect of melatonin, by exhibiting antioxidant, antiapoptotic and anti-inflammatory effects, in brain tissue during endotoxemia. The authors would like to thank the Ministry of Science of the Republic of Serbia(project:451-03-47/2023-01/200113).

Keywords: Lipopolysaccharide, Melatonin, Oxidative stress, Apoptosis, Inflammation, Brain

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Severe Obstructive Sleep Apnea in Musk-Positive Myasthenia Gravis: A Rare Presentation of a Rare Disease?

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Background: Myasthenia gravis (MG) is a chronic autoimmune disorder of the neuromuscular junction characterized by fluctuating weakness of the ocular, bulbar, limb and respiratory muscles. MG with MuSK antibodies is more often associated with bulbar involvement and has a higher frequency of respiratory failure and myasthenic crises. Increasing evidence suggests a link between breathing sleep disorders such as obstructive sleep apnea (OSA) and MG.

Case presentation: We present the case of a 58-year-old female admitted to our hospital for isolated, severe, hypoxemic and hypercapnic respiratory failure

that required noninvasive ventilation. The patient had been diagnosed with MuSK-positive MG, but denied fatigability, weakness, and other relevant symptoms over the past 20 years, despite not taking any immunosuppressive or anticholinesterase medication. The respiratory failure improved with corticotherapy and pyridostigmine. The sleep polygraphy performed after stabilization showed severe OSA (31 episodes of apnea-hypopnea per hour). A month later, the patient had another exacerbation compatible with myasthenic crisis, this time accompanied by bulbar deficits and limb weakness, that was successfully treated with plasma exchange therapy. Long-term treatment with pyridostigmine, oral methylprednisolone and azathioprine was started, with favorable outcome over the following year, apart from the further worsening of the OSA syndrome.

Conclusion: Our case reveals severe OSA in a normoponderal, middle aged, non-smoking, white female who has MuSK-positive MG with predominant respiratory muscle involvement. OSA is more prevalent among myasthenic patients compared to the general population, being encountered even in those without classical risk factors.

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Systemic Lupus Erythematosus transverse myelitis: a case report and literature review

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Introduction: Systemic lupus erythematosus (SLE) is an autoimmune disease which involves multiple organs. A severe complication of SLE is transverse myelitis (TM), affecting around 1-2 % of patients. The most frequent type of TM is longitudinal extensive myelitis (LETM) that includes three or more spinal cord segments on magnetic resonance imaging (MRI). The earlier an agressive treatment is introduced, the better the long- term prognosis of patients with TM is.

Methods: Clinical case report of a patient with a relapse of SLE TM and literature review.

Results: 34 years old woman was admitted to the emergency department because of progressing tetraparesis, fever, headache and double vision. It was known from anamnesis that patient was diagnosed with SLE and had thoracic TM in 2015. Paraplegia and anesthesia of lower limbs and sphincter dysfunction remained after the first episode of TM. Examination revealed manifestation of coarse paraparesis of upper limbs. Lymphopenia, low complements, antiphospholipid syndrome, high titer of antibodies to double - stranded DNA and erythrocyte sedimentation rate was noted. Spine MRI showed C1-Th4 LETM. Other causes and possible comorbidity were ruled out. Treatment with pulse steroids and cyclophosphamide was initiated. In the absence of response to treatment intravenous human immunoglobulin and rituximab was continued. As a result, recovering hand strength was observed.

Conclusions: This case report shows the necessity of multidisciplinary cooperation in diagnosing and treating patients with TM, even though it remains controversial how widely investigation in this patient group should be performed.

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Factors associated with working status in persons with Neuromyelitis Optica Spectrum Disorders

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Aim: Neuromyelitis Optica Spectrum Disorders (NMOSD) can substantially affect employment and work-related outcomes. The present study aimed to explore factors associated with working status in persons with NMOSD (pwNMOSD). To the best of our knowledge, this is the first investigation dealing with this issue in NMOSD.

Methods: Fifty-four pwNMOSD, who fulfilled the 2015 NMOSD criteria, diagnosed and followed at the Clinic of Neurology, University Clinical Center of Serbia, Belgrade, were included in the cross-sectional study. The data related to the work status of

pwNMOSD were collected by questionnaire. Severity of the disease was evaluated by the Expanded Disability Status Scale (EDSS). Presence of depressive symptoms, fatigue and pain were measured by the Beck Depression Inventory (BDI), Fatigue Impact Scale (FIS) and Pain Assessment Questionnaire, respectively.

Results: From the cohort of 54 pwNMOSD enrolled in the study, 42.6% were employed, and of those unemployed, 38.9% attributed their unemployment to the health-related issues. Multivariate logistic regression analysis showed that factors statistically significantly associated with unemployment status in our pwNMOSD were: higher level of disability measured by EDSS (OR=1.95, 95% CI=1.29-2.96, p=0.002), longer duration of the disease (OR=1.15, 95% CI=1.01-1.31, p=0.030), and lower level of education (OR=0.75, 95% CI=0.57-0.98, p=0.048).

Conclusions: In our study, predictors of unemployment in pwNMOSD were level of physical disability, duration of disease, and level of education. Treatment and interventions targeting these factors in pwNMOSD may be effective in helping individuals maintain employment.

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Frequency of comorbidities in patients with neuromyelitis optica spectrum disorder: the Serbian national registry data

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Aim: Neuromyelitis optica spectrum disorder (NMOSD) is associated with various comorbidities, including non-autoimmune and autoimmune conditions. The aim of this study was to investigate the frequency of autoimmune comorbidities in the Serbian NMOSD cohort.

Methods: The data on the demographic and clinical characteristics of NMOSD patients was obtained from the Serbian national NMOSD Registry. All patients fulfilled the 2015 NMOSD criteria. Severity of the disease was evaluated by the Expanded Disability Status Scale (EDSS). The frequency of comorbidities was compared between anti-aquaporin 4 antibody (AQP4-IgG) seropositive and seronegative patients.

Results: A total of 141 NMOSD patients were enrolled. The ratio of women to men was 4.2:1. The median age at onset was 40 years (range 4–73), and mean duration of the disease was 8.2+/-7.4 years. The median EDSS score at the last follow-up visit was 4.0 (range 0.0-10.0). Seventy-two (51.1%) patients reported at least one comorbidity. Fifty-one patients (36.2%) had autoimmune comorbidities: the most common disorders were autoimmune thyroiditis (N = 17; 11.1%), Sjogren's disease (N = 13; 9.2%), systemic lupus erythematosus (N = 7; 5.0%), and myasthenia gravis (N = 5; 3.5%). A significantly higher frequency of autoimmune comorbidities was observed in the AQP4-IgG positive patients (p=0.009). Autoimmune comorbidities were significantly associated with AQP4-IgG positivity (OR=3.2, 95% CI=1.3-7.5, p=0.009).

Conclusion: Our results show that half of the patients had comorbidities, suggesting screening for comorbidity as part of NMOSD care.

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Acute demyelinating encephalomyelitis (ADEM) in adults: postinfectious encephalomyelitis or something else?

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Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a rare, antibody-mediated inflammatory demyelinating disorder of the central nervous system presented by various phenotypes that may vary with age, such that ADEM-like lesions are more likely to affect children, whereas optic neuritis and myelitis tend to be more common among adults.

Case presentation: We report the case of a 28 years old female presented to the Emergency Department

with a 3-day history of fever, leg weakness and numbness, imbalance, gait disturbances and difficulty urinating. The neurological examination revealed conductive hypoesthesia from Th4-Th5 level, mild paraparesis with muscle hypotonia and hyperreflexia, Babinski reflex, severe ataxia, positive meningeal signs, and urinary retention. Contrast-enhanced MRI of the brain and spinal cord revealed transverse myelitis with extensive spinal cord involvement from C3 to the conus medullaris, and cerebral lesions with demyelinating appearance in the optic thalamus, parietal, periaqueductal, medulla oblongata, pons, area postrema. Cerebrospinal fluid (CSF) analysis demonstrated lymphocytic pleocytosis (160 cells, 98% lymphocytes, protein 0.99 g/L). PCR tests for EBV, CMV, HSV1, HSV2, and enterovirus in CSF were negative. Oligoclonal bands were negative. Immunological screening revealed positive serum anti-MOG and negative anti-aquaporin 4 antibodies. The patient received intravenous Methylprednisolone 1 g/day for 5 days and progressive improvement was noticed. After discharge she continued with Prednisolone 1 mg/kg/day, with complete resolution of symptoms after one month.

Conclusion: MOGAD is a rare demyelinating pathology and is rarely presented with ADEM in adults. In this case it was important to do a differential diagnosis with NMOSD (neuromyelitis optica spectrum disorders) and MS (multiple sclerosis) in order to establish the treatment as well as the prognosis that seems to be more favorable in case of MOGAD.

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Isolated neurosarcoidosis presenting as an extensive form of encephalomyelitis

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Introduction: Sarcoidosis is a systemic inflammatory disease affecting multiple organs. Neurosarcoidosis, especially as an initial and isolated presentation, is rare, diagnostically challenging and potentially life-threatening when the lesions are extended cerebromedullary, as reported in this case.

Methods: A 46-year-old woman presented in our clinic with paraparesis, speech impairment, action tremor and seizures, developed progressively over 3 months. The initial magnetic resonance imaging (MRI) examination, humoral tests and lumbar puncture pointed to an ill-defined inflammatory disease of the central nervous system. Further workup included full-body positron emission tomography and computed tomography and brain biopsy.

Results: Cerebral and medullary MRI revealed extensive white matter lesions in the left cerebral hemisphere with mass effect and a longitudinal lesion covering 11 vertebral segments with heterogeneous contrast enhancement. Cerebrospinal fluid (CSF) examination revealed 104 cells/microliter (99% mononuclear), elevated proteins, moderately low glucose and the absence of oligoclonal bands or microbial agents, including Mycobacterium tuberculosis. Systemic autoimmunity screening, antiMOG and antiAQP antibodies, onconeural antibodies, CSF GFAP antibodies, tumoral markers, serum angiotensin-converting enzyme and interleukin2 receptor tested negative. No lesions were found in other organs. The brain biopsy showed no evidence of lymphoma, vasculitis or primary angiitis of the central nervous system, but was highly suggestive of neurosarcoidosis. Evolution was promptly favourable under corticosteroids.

Conclusion: Isolated neurosarcoidosis is uncommon in clinical practice and can be difficult to diagnose. In this case, despite the initial severity, the disease was monophasic and most symptoms remitted under corticotherapy. Overtime management required immunosuppressive therapy.

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Treatment dilemmas of neuro-tuberculosis: Paradoxical response

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Introduction: Neuro-tuberculosis, particularly meningeal tuberculosis, poses a persistent global health challenge with cases demonstrating clinical dilemmas. This study addresses the complex issue of treatment escalation in clinically asymptomatic patients with persistent cerebral-spinal fluid (CSF) reactivity and worsening imaging findings.

Case report: A 24-year-old university girl initially treated for Kikuchi disease with immunomodulatory therapy was later diagnosed with smear-positive pulmonary tuberculosis after two months. Despite initiating CAT1 anti-TB treatment, she experienced recurrent fever, meningitic symptoms, and new focal neurological signs and was ultimately diagnosed with meningeal TB. Complications included multiple tuberculomas and cerebral venous sinus thrombosis, necessitating the escalation of glucocorticoid treatment and a switch to individualized anti-tuberculosis drugs.

After ten months of treatment, despite clinical wellness, the patient exhibited persistently reactive CSF and a large tuberculoma mimicking an abscess. In a multidisciplinary decision-making process, brain biopsy before second-line immunotherapy with thalidomide or infliximab was considered, but the patient declined. Tailoring off immunotherapy based on clinical resolution led to discontinuation of anti-TB treatment after 18 months, resulting in gradual lesion resolution. The patient presently functions well without disability or cognitive impairment.

Conclusion: This case highlights the challenge of managing paradoxical response in central nervous system tuberculosis. It underscores the need for further studies to determine the optimal timing and extent of treatment in such cases.

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The great pain of small fiber neuropathy: a case of immune-mediated small fiber neuropathy

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Introduction: Small fiber neuropathy (SFN) is the result of somatosensory and autonomic A-delta and C fibers injury. Although most of the cases are idiopathic, SFN may also occur due to metabolic, immune-mediated, infectious, hereditary, or toxic etiologies. In idiopathic SFN, the fibers are usually involved in a length-dependent manner, whereas a non-length-dependent distribution would rather suggest a paraneoplastic or immune-mediated pathology.

Methods: A 31-year-old woman, diagnosed with mixed connective tissue disease one year prior and undergoing combination therapy with corticosteroids and mycophenolate mofetil, was admitted to our clinic for diffuse burning pain, tingling and numbness, primarily in the palms and soles. She also complained of recent gastrointestinal disturbances, orthostatic dizziness and palpitations, fatigue, and general malaise. Neurological examination revealed mild proximal tetraparesis and normal sensory examination and tendon reflexes.

Results: An extensive work-up for metabolic (diabetes, vitamin B12 deficiency, hypothyroidism), infectious (HIV, hepatitis C, Lyme disease), hereditary and immune-mediated diseases was performed, revealing positive anti-dsDNA and anti-U1RNP antibodies. Apart from minimal myopathic changes, the electroneuromyography results were unremarkable. Subsequently, SUDOSCAN revealed prominent sudomotor dysfunction highly suggestive of small fiber neuropathy, most probably secondary to mixed connective tissue disease. The patient received intravenous immunoglobulin (2g/kg), with marked symptomatic improvement within days.

Conclusions: Small fiber neuropathy should be suspected in patients presenting with positive sensory phenomena and autonomic dysfunction who have normal nerve conduction studies. Furthermore, patients should be thoroughly screened for reversible causes of small fiber neuropathy and benefit from appropriate etiological and symptomatic treatment.

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Immune reconstitution for the treatment of myasthenia gravis- the case for cladribine

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Autoimmune myasthenia gravis (MG) is a neuromuscular junction (NMJ) disorder marked clinically by fatigable muscle weakness and serologically by the presence of autoantibodies. Autoantibodies against acetylcholine receptors (AChRs), muscle-specific kinase (MuSK), and lipoprotein-related protein 4 (LPR4) have been proven to be pathogenic.

Pathological B- and T-cell subtypes are implicated, including memory B and plasma cells, with concomitant reduced regulatory B(reg) and Treg cells activity. This implicates that acting selectively on pathogenic T and B cells might be important strategy to suppress MG activity in order to prevent the downstream damage in the neuromuscular junction.

Immune reconstitution IIR) has become attractive approach to control different types of autoimmune diseases with multiple sclerosis as the best studied condition. Cladribine is one of the prototype drugs to induce IR with long lasting therapeutic effects (Giovannoni and Mathews, 2022).

It was tempting to use CLAD in MG patients to test this hypothesis. Indeed, in the first pilot clinical study we demonstrated the efficacy together with appreciable safety profile of cladribine (Rejdak et al., 2018). Initial findings encouraged us to organize randomized, double blind placebo controlled trial currently being conducted in 9 clinical centers in Poland. In this presentation the study rationale and design of ongoing trial (EudraCT Number: 2020-005762-34) will be discussed.

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Focused ultrasound thalamotomy for tremor due to chronic inflammatory demyelinating polyneuropathy

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Background: Unilateral MRI-guided focused ultrasound (FUS) ablation has established efficacy in tremor relief.

Objective: To describe a patient that underwent FUS thalamotomy for tremor due to chronic inflammatory demyelinating polyneuropathy (CIDP).

Methods: Tremor was assessed in the treated hemibody using the Clinical Rating Scale for Tremor (hemi-CRST).

Results: A 63-year-old male suffered from severe disabling tremor for 8 years due to CIDP. He had marked sensorimotor impairment. He was offered FUS treatment. Immediately following treatment there was improvement in tremor, from a baseline hemi-CRST score of 14 to a score of 7. At 1 month tremor had partially returned with a hemi-CRST score of 11. At 6 months tremor was almost as severe as before treatment with the hemi-CRST score rising to 13 and remaining unchanged at 1 year. The patient reported subjective gait unsteadiness and lip parasthesias that resolved within 1 month.

Conclusions: To the best of our knowledge this is the first report of a single patient who underwent FUS thalamotomy for tremor due to CIDP. Our experience does not support the use of this technology in this condition.

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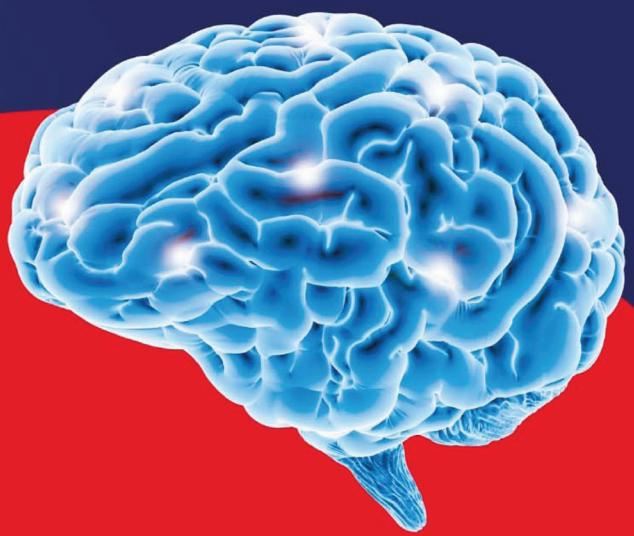

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The role of mitophagy in the pathogenesis of ischemic stroke

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Objective: More and more studies have shown that mitochondrial autophagy has a close relationship with the occurrence of cerebral ischemic stroke (CIS). Therefore, this paper reviews the mechanism of mitochondrial autophagy in the development of CIS.

Methods: In this paper, we searched the databases of China Knowledge Network, Web of Science, PubMed, and other databases with the keywords "ischemic stroke" and "mitochondrial autophagy" by the method of literature search, and collected and analyzed the relevant literature in recent years.

Results: The expression of NIX and BNIP3, as mitochondrial autophagy receptors in mammalian cells, is upregulated during the onset of ischemic stroke, which activates mitochondrial autophagy to ameliorate brain injury due to CIS. However, overregulation of BNIP3 during ischemia-reperfusion leads to cell death. PINK1/Parkin, a classical pathway of mitochondrial autophagy, can play an anti-apoptotic, anti-inflammatory, and anti-oxidative stress role after the occurrence of CIS by regulating its expression level.

Conclusions: Mitochondrial autophagy is activated during CIS and acts on other related pathological processes by removing damaged mitochondria, which are closely linked to biological processes such as apoptosis, oxidative stress, and inflammation in cells, thus affecting neuronal cell survival and death. Mitochondrial autophagy acts as an early defense mechanism after the onset of CIS to remove damaged mitochondria in a timely manner and reduce stimulation and damage to normal mitochondria, but when autophagy is excessive or blocked, it may exacerbate the damage. Therefore, as a double-edged sword, the mitochondrial autophagy process is expected to be a new target for the treatment of CIS.

Keywords: Mitophagy; Ischemic stroke; BNIP3
Funding: NNSF of China (82004028); Shanxi Science and Technology Innovation Young team Project (202204051001028); Shanxi University of Chinese Medicine Young scientists training Project (2021PY-QN-09); Shanxi University of Chinese Medicine discipline Construction funds (2023XKJS-02);Datong City Applied Basic Research Program Project (2022066).

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The impact of astrocytes on the immune response of stroke

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Objective: After ischemic stroke (IS), a cascade of reactions is triggered, leading to inflammation and immune responses. Astrocytes (Ast), as the primary glial cells in the central nervous system, play a crucial role in maintaining brain homeostasis.

Method: Activated Ast can increase the uptake of extracellular glutamate and sodium/potassium-ATP enzyme activity, improving the reconstruction of the blood-brain barrier during the acute phase of IS. Ast also secretes chemotactic and adhesion molecules, regulating the activity and function of immune cells, and influencing inflammation development. Ast can interact with neurons, phagocytizing and degrading

apoptotic neurons and cell fragments, playing an important role in immune surveillance and clearance. Therefore, Ast is crucial in regulating brain immune and repair functions, controlling inflammation and immune responses, as well as promoting neuronal repair and regeneration. Additionally, Ast can undergo reactive astrocytosis after IS, isolating lesions and limiting neuroinflammation, but also impeding axonal regeneration. Reactive Ast can also interact with microglia to release pro-inflammatory substances, causing secondary neuronal damage. However, the removal of Ast will result in neuron survival. Results: Ast can take up extracellular glutamate, release neurotrophic factors, and stabilize extracellular fluid and ion homeostasis, displaying neuroprotective effects. Similar to microglia, Ast has a dual role in the immune response.

Conclusion: Ast plays a neuroprotective role in IS.

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Delayed Treatment Resulted in a Better Outcome in Spontaneous Spinal Epidural Hematoma: Case Report

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Spontaneous Spinal Epidural Hematoma (SSEH) is a rare but potentially devastating medical emergency characterized by the accumulation of blood in the epidural space surrounding the spinal cord.

A 65-year-old male presented with sudden stabbing back pain and stiffness, which gradually progressed to complete paraplegia with bladder dysfunction four days before came to the hospital with no risk factors related. Magnetic Resonance Imaging (MRI) showed epidural hematoma. The patient underwent surgery to remove the hematoma and laminectomy for decompression. After five weeks in the hospital with appropriate and consistent rehabilitation, the patient's symptoms improved significantly postoperatively, leading to discharge.

Spinal epidural hematoma remains a rare but critical condition that requires prompt recognition and intervention to optimize patient outcomes.

Keywords: Spinal epidural hematoma, Rehabilitation, neurologic deficit

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Inherited neurological disorders in Consanguineous families in Palestine and Israeli Arabs

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Consanguinity leads to a high prevalence of autosomal recessive disorders in inbred populations. Arab community in Israel and the Palestine are an example, but specialized medical care is limited in Palestine. Genetic diagnosis and genetic counseling with specific treatment are a must. In this study whole-exome sequencing as a first-line diagnostic tool in 83 Palestinian and Israeli Arab families with suspected neurogenetic disorders was performed and probable genetic diagnosis was established in 51% of the families (42 families). Pathogenic, likely pathogenic or highly suggestive candidate variants were found in the following genes extending and refining the mutational and phenotypic spectrum of these rare disorders: ACO2, ADAT3, ALS2, AMPD2, APTX, B4GALNT1, CAPN1, CLCN1, CNTNAP1, DNAJC6, GAMT, GPT2, KCNQ2, KIF11, LCA5, MCOLN1, MECP2, MFN2, MTMR2, NT5C2, NTRK1, PEX1, POLR3A, PRICKLE1, PRKN, PRX, SCAPER, SEPSECS, SGCG, SLC25A15, SPG11, SYNJ1, TMCO1, and TSEN54. Thus, this cohort has proven to be optimal for prioritization of new disease genes. Two separately published candidate genes (WWOX and PAX7) were identified in this study. Analyzing the runs of homozygosity (ROHs) derived from the Exome sequencing data as a marker for the rate of inbreeding, revealed significantly longer ROHs in the included families compared with a German control cohort. The total length of ROHs correlated with the detection rate of recessive disease-causing variants. Identification of the disease-causing gene led to new therapeutic options in four families. Finally, the results of the study carry consanguinity awareness for affected families and to health policy makers.

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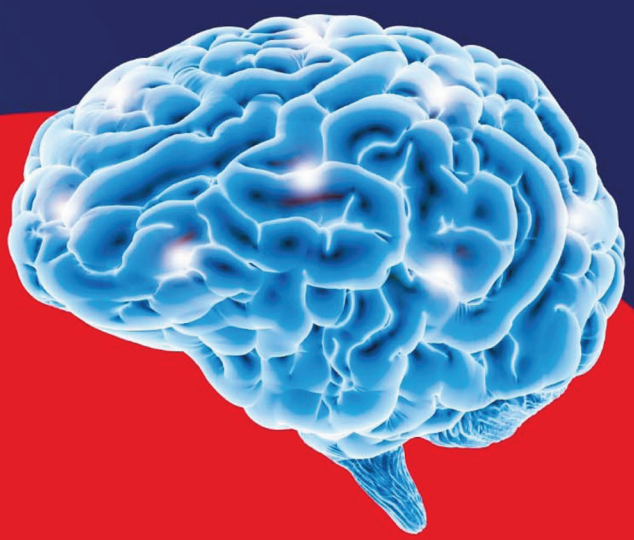

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Comparative Safety of Istradefylline among Parkinson's Disease Adjunctive Therapies: A Systematic Review and Meta-Analysis of Randomized Controlled Studies

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Istradefylline has demonstrated a significant reduction in "OFF" time when used as an adjunct to levodopa/carbidopa in patients with Parkinson's disease (PD). A systematic review was updated with additional RCTs 1/1/2010-4/15/2019 to evaluate the safety of istradefylline vs. other PD adjuncts. Pairwise meta-analysis and Bucher indirect comparisons were used to generate estimates of relative safety. Results are presented as OR [95% CI] relative to istradefylline. Overall, 57 RCTs involving 11,517 patients were included for meta-analysis. Istradefylline data were extracted from clinical study reports. At 40mg, istradefylline demonstrated significantly lower odds of dyskinesia and somnolence compared to dopamine agonists (DAs) (1.30 [1.01, 1.69] and 2.50 [1.28, 5.00]) and lower odds of hypotension compared to monoamine oxidase type B inhibitors (8.33 [1.67, 50.00]). At 20mg, the odds of dyskinesia were significantly lower for istradefylline vs. catechol-O-methyl transferase (COMT) inhibitors (1.52 [1.09, 2.13]), DAs (1.61 [1.16, 2.22]), and all interventions (1.45 [1.06, 2.00]). Relative to istradefylline, amantadine had significantly increased odds of hallucinations (40mg: 3.57 [1.30, 10.00]; 20mg: 4.76 [1.64, 14.29]), and insomnia and withdrawals due to treatment emergent adverse events (TEAEs) at 20mg (8.33 [1.06, 50.00] and 2.86 [1.18, 6.67]). The odds of overall incidence of TEAEs including constipation, dyskinesia, hallucination, hypotension, insomnia, orthostatic hypotension, and somnolence were significantly lower for istradefylline compared with COMT inhibitors (40mg: 1.33 [1.03, 1.75]; 20mg: 1.32 [1.01, 1.72]) and amantadine (40mg: 3.45 [1.85, 6.25]; 20mg: 3.33 [1.82, 6.25]). Istradefylline is associated with a generally favorable safety profile relative to other adjunct medications in this study.

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Real-world benefits of APO-go® POD in advanced Parkinson's disease (PD) – a patient case study

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Background Continuous subcutaneous apomorphine (APO) infusion is an effective and well-tolerated therapy for advanced PD. APO-go® infusion (Britannia Pharmaceuticals) is administered using a portable mini-pump with the solution contained in pre-filled syringes (PFS). A new method of administration, APO-go® POD, is now available with the solution supplied in a cartridge. The first UK patient was initiated in 2023.

Methods The practical benefits of APO-go® PFS and POD administration are compared, and illustrated with a case study from our centre of a patient who transitioned from PFS to POD.

Results The time required to set up the infusion with APO-go® POD is 34 seconds (8 steps), compared to 1 minute 48 seconds for PFS (12 steps), a reduction of 1 minute 14 seconds. The POD system requires fewer ancillaries and does not require liquid transfer as it attaches directly to the pump. At our centre, a 52-year-old female patient who had had PD for 10 years commenced APO-go® PFS infusion in January 2023. This effectively controlled her symptoms, but with impaired dexterity she struggled with the set-up (liquid spillage) and disposal of ancillaries, particularly when travelling. She feels that the transition to POD has saved her time, is easier to set up in the morning, and there is less wastage.

Conclusions This case highlights the practical benefits the POD system can provide for PD patients in their daily lives. Set-up time and steps are reduced with the POD system, streamlining the administration process, making it easier for patients, and promoting independence.

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What change to expect in duration of benefit per dose when switching from IR CD-LD to IPX203 (ER CD-LD)

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Objective: To investigate if duration of benefit ("Good On" time) per dose during immediate-release (IR) carbidopa-levodopa (CD-LD) treatment predicts response to IPX203 conversion.

Background: IPX203, a novel oral extended-release (ER) CD-LD capsule, was developed to address levodopa's limited absorption window and short plasma half-life.

Methods: We performed post hoc analyses on Hauser diary data from 495 subjects who completed the RISE-PD phase 3 clinical trial. The patient population was rank-ordered and divided into quartiles based on "Good On" time per dose at the end of IR CD-LD dose optimization. Mean end of study (EOS) "Good On" time per dose values were then compared between IPX203 and IR CD-LD–treated groups for each quartile.

Results: Mean "Good On" times per dose for each quartile at the end of the IR CD-LD dose optimization phase were 1.35, 1.91, 2.36, and 2.96 hours. For IR CD-LD patients, EOS mean "Good On" times per dose were 1.71, 2.06, 2.34, and 2.93 hours. For IPX203 patients, EOS mean "Good On" times per dose were 3.16, 3.44, 4.02, and 4.55 hours. Mean differences in "Good On" time per dose between IPX203 and IR CD-LD were 1.53h, 1.38h, 1.85h, and 1.56h for each quartile, respectively.

Conclusions: Regardless of the duration of efficacy observed with IR CD-LD, measured as "Good On" time per dose, the improvement in duration of benefit observed with IPX203 remained similar, with an overall mean increase of 1.58 hours per dose. These results may help care providers plan conversion regimens and anticipate clinical responses.

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Parkinson's Disease, a Long-term Sequela of Neurogenic Orthostatic Hypotension with Cardiac Sympathetic Denervation

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Introduction: Idiopathic neurogenic orthostatic hypotension is a rare disorder of the autonomic nervous system that significantly impacts the quality of life. The natural history of neurogenic orthostatic hypotension varies and may evolve into a central synucleinopathy. There is a need for robust and pathophysiologically relevant biomarkers of preclinical central synucleinopathies. In this report, we describe the long-term follow-up of patients with neurogenic orthostatic hypotension and imaging evidence of cardiac sympathetic denervation by 123I-metaiodobenzylguanidine single photon emission tomography (Cardiac 123I-MIBG SPECT)

Methods: Patients with orthostatic hypotension underwent clinical autonomic evaluation and were diagnosed with idiopathic neurogenic orthostatic hypotension. Cardiac 123I-MIBG SPECT was performed as part of the diagnostic algorithm to assess sympathetic innervation. Ten patients with neurogenic orthostatic hypotension had cardiac sympathetic denervation and were followed for the development of Parkinson's disease or neuroimaging evidence of central dopamine deficiency by 18F-DOPA positron emission tomography.

Results: During a mean follow-up of 5.6 years, all patients showed clinical or neuroimaging signs of central dopamine deficiency: Seven were diagnosed with Parkinson's disease; three showed non-diagnostic minimal extrapyramidal signs with unilaterally reduced 18F-DOPA-uptake. Among 5 patients tested for genetic mutations related to Parkinson's disease, four were GBA mutation carriers.

Conclusions: In this series, the majority of patients with neurogenic orthostatic hypotension and imaging evidence of cardiac sympathetic denervation progressed to Parkinson's disease during follow-up, and the remainder developed clinical or neuroimag-

ing evidence of nigrostriatal dopamine deficiency. This form of neurogenic orthostatic hypotension represent a body-first course toward Parkinson's disease via the sympathetic route.

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Long-term follow-up of patients with advanced Parkinson's disease treated with levodopa–entacapone–carbidopa intestinal gel infusion (LECIG) in Sweden

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Background: Levodopa–entacapone–carbidopa intestinal gel infusion (LECIG) was approved by the Swedish Medical Products Agency in 2018 for the management of advanced Parkinson's disease (PD). We previously reported initial experience with LECIG treatment at our centre in 24 patients treated for a median of 305 days.1 Here we report long-term data for this cohort who have been treated with LECIG for up to four years.

Methods: A retrospective, observational study of 24 patients (11 female, 13 male). Medical records were examined regarding gender, age, time since PD diagnosis, LECIG treatment duration, LECIG infusion dosage, adverse events and device complications.

Results: Patients had a mean duration of PD of 16 years and a mean age of 69.2 years at the start of LECIG treatment. Of the original 24 patients, 10 remain on LECIG treatment and one has paused due to problems with gastrointestinal access. Mean time on treatment is currently 26.5 months, with 10 patients continuing LECIG treatment. To date, three patients have received LECIG treatment for over four years. Of the 14 patients who stopped treatment, eight died. Three patients stopped during treatment initiation due to diarrhoea. Of the patients still receiving treatment, the most recent PDQ-8 score taken had a median of 12.

Conclusions: Our study is the first to present long-term data on the use of LECIG for up to four years in patients with advanced PD and indicates that it is generally well-tolerated in long-term treatment.

Reference 1. Öthman M, et al. J Pers Med. 2021;11(4):254.

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Prescription patterns in treatment of Parkinson's disease in tertiary centers in Poland

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There are several medications available for Parkinson's disease treatment. The approach to the pharmacotherapy has been modified due to levodopa phobia two decades ago and dopamine agonist phobia recently. The aim of our observational, retrospective, multicenter study was to show how PD specialists in Poland treat PD patients nowadays and how the literature warnings influenced their practice. 494 patients took part in our study (Male: 301, Female: 193). Their mean age was 64.75 years (SD 10.62, 27-89), mean H-Y score was 2.45 (SD 0.68, 1-5) and mean duration of the disease was 9.54 years (SD 5.80, 1-30). 465 patients were treated with LD (mean dose 810.58mg), 292 with DA (ropinirole – 176 (mean dose 8.64mg), pramipexole – 105 (mean dose 1.76mg), piribedil - 8, rotigotine - 3), 202 with MAO-B inhibitors (rasagiline 198, selegiline 4), 197 with amantadine, 7 with entacapone and 4 with anticholinergics. 119 patients were on PD monotherapy, 152 were treated with two medications and 223 were treated with three or more drugs for PD. Patients were divided into subgroups depending on their HY score, age and duration of the disease, then pharmacotherapy of each group was analyzed showing that in every group levodopa

was most often prescribed drug and remains a gold standard in treatment of PD in tertiary centers in Poland. Dopamine agonists were the second most frequently prescribed group of medications in our study, although they were less frequently used in older population (70 years old) and with HY score of 3 or more.

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Multiparametric cerebellar radiomic biomarkers for diagnosing Parkinson's disease

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Objectives: A growing body of research has provided clinical, pathological, and neurophysiological findings, unequivocally establishing a link between the cerebellum and Parkinson's disease (PD). This study aimed to investigate the diagnostic potential of multiparametric magnetic resonance imaging (MRI) radiomics derived from the cerebellum.

Methods: This retrospective study collected data (n=618) from two datasets. The Parkinson's Progression Markers Initiative (PPMI) provided the training set, comprising healthy controls (HC, n=156) and PD patients (n=162). The results were subsequently validated using the test set data from an in-house dataset in Dalian, China, which included 146 controls and 154 PD patients. MRI radiomic features (n = 883) were extracted from the grey and white matter of the cerebellum. Three diagnostic models were developed: a cerebellar gray matter model, a cerebellar white matter model, and a combined cerebellar gray and white matter model.

Results: The area under the receiver operating characteristic curve (AUC) analyses revealed that the combined model (AUCs 0.987; Sensitivity 0.951; Specificity 0.911) demonstrated superior predictive performance compared to the gray matter model (AUCs 0.897; Sensitivity 0.873; Specificity 0.921, p = 0.0392) and white matter model (AUCs 0.892; Sensitivity 0.863; Specificity 0.921, p = 0.0486) in the training set. Noteworthy radiomic features contributing to PD development included dependence variance and run variance domains in the white matter, as well as mean squared and gray level normalized domains in the gray matter.

Conclusions: In conclusion, this study underscores multiparametric cerebellar MRI radiomics may have an incremental diagnostic value as a biomarker for PD.

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Role of rhythm perception and posture disturbances in daily life of patients with Parkinson's disease

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Walking disability in Parkinson disease is secondary to hypometric stride, postural and rhythmic disturbances. However, there is significant heterogeneity between patients which is rarely taken into account in rehabilitation.

Methods: Several studies have been carried out on different patient populations 1. Assessment of difficulties in performing rhythmic movements in daily life using specific self-questionnaires 2. Evaluation of the abilities of perceive and reproduce rhythms with BASTAA battery (Battery for the Assessment of Auditory Sensorimotor and Timing Abilities) 3. Evaluation with the miniBEST scale of postural abilities in patients with freezing 4. Impact of a serious game on rhythmic activities (walking and speaking).

Results: Parkinson's patients may have early difficulties to perform rhythmic motor movements that impact daily life. These disorders can be detected by a self-questionnaire or measured by a BAASTA battery. Freezing is responsible for falls only in the presence of abnormalities in postural control. The anomalies also concern to the perception of rhythm. Serious games developed to train the motor and sensory sides of rhythm improve speaking and walking skills.

Discussion: All of this work confirms the importance of rhythmic difficulties in the speech and walking disorders observed in Parkinson's patients.

It is therefore necessary to develop complete rehabilitation programs combining classic physiotherapy sessions with rehabilitation exercises and training of rhythmic skills using new technologies and the principles of therapeutic education. As postural disorders condition the risk of falling, it will be necessary for these patients to combine specific postural rehabilitation programs.

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Focused ultrasound rescues Parkinson patient following removal of implanted DBS hardware

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Background: Unilateral MRI-guided focused ultrasound (FUS) ablation has established efficacy in Parkinson's disease (PD). The pallidothalamic tract is gaining popularity as the target of choice.

Objective: To describe a single patient that underwent FUS pallidothalamic tractotomy for advanced PD following DBS hardware removal.

Methods: We present a patient with advanced PD and disabling symptoms that underwent FUS after removal of DBS due to severe infection. Unified PD Rating Scale (UPDRS) score in ON state was documented before and after the procedure.

Results: A 62 year old woman with a 12 year duration of PD underwent DBS 5 years previously at another center. She presented at our center with severe cellulitis and osteomyelitis at the electrode insertion site. After repeated antibiotic treatments with no improvement, DBS hardware was removed. Medication adjustments did not improve symptoms, while others, including apomorphine, caused psychosis. ON state UPDRS score was 37 with the patient suffering from severe rigidity and unable to stand due to impaired balance. As rescue treatment, unilateral FUS pallidothalamic tractotomy was performed. Following this procedure, ON state UPDRS score was decreased to 22. She was able to walk with no difficulty. No side effects were reported.

Conclusions: To the best of our knowledge this is the first case report demonstrating efficacy and safety of FUS pallidothalamic tractotomy in PD following removal of DBS hardware. Long term follow up is needed. FUS may offer hope for PD patients unwilling or unable to undergo DBS. Larger studies are needed to substantiate our findings.

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Type 2 Diabetes Mellitus comorbidity among Parkinson's disease patients: A community based big-data study

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Background: Recent studies investigating the relationships between Parkinson's Disease (PD) and Type 2 Diabetes Mellitus (T2DM) report inconclusive results, possibly due to small cohorts and disregard for the timing order of T2DM and PD diagnoses.

Objectives: To compare the risk of T2DM among a large-scale cohort of PD patients, to that of the general population, and to evaluate the effect of T2DM occurrence on PD patients` survival.

Methods: A population-based, large-scale cohort study, of incident PD patients members of Maccabi Health Services (MHS), a large Israeli HMO, who initiated anti-parkinsonian medications between 1.1.2000 and 12.31.2018. T2DM occurrence was collected from MHS T2DM-registry. Standardized-Incidence-Ratio (SIR), accounting for age, chronological-year, and sex, was calculated to compare

T2DM risk in PD patients to that in the general MHS population. Cox regression was used to estimate the hazard ratio (HR) for death.

Results: The PD cohort comprised 11253 patients, 54.7% men, average age at PD diagnosis of 71(SD=11). Average follow-up was 6.8years (SD=4.5). During the study period, 3823 (33.97%) patients were diagnosed with new T2DM.prevalent T2DM in the PD cohort was significantly lower when compared to the reference population SIR=0.68 (95%CI; 0.66- 0.70). Out of 7976 patients, with no T2DM diagnosis at PD diagnosis. 666 (8.4%) developed T2DM during follow-up, and T2DM occurrence decreased their death risk HR= 0.70 (95%CI 0.62-0.78).

Conclusion: T2DM incidence and treatment apparently decrease PD incidence, risk, and death. Further studies are needed to investigate the cause for these findings, for potential implications for PD clinical management and prognosis.

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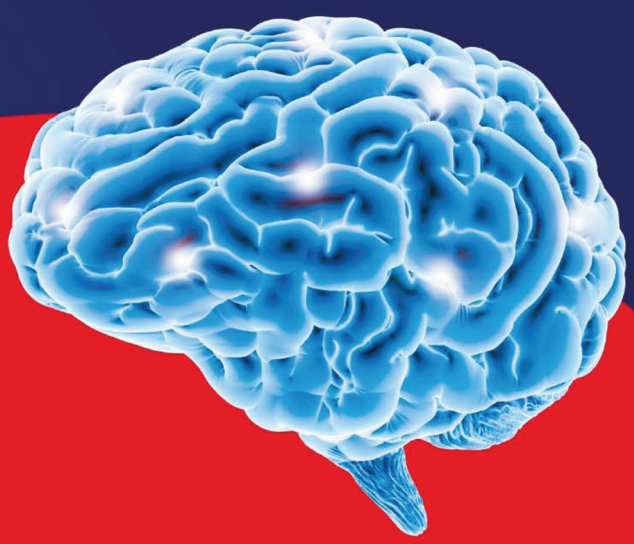
Rehabilitation



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Naphthalan therapy in the rehabilitation of patients with gunshot injuries of peripheral nerves

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Target. To study the effectiveness and mechanisms of action of naphthalan therapy (NT) in the rehabilitation of patients with gunshot injuries of peripheral nerves (GIPN).

Material and research methods. Clinical, electromyographic (EMG) and rheovasographic (RVG) studies were carried out on 48 patients with GIPN of the upper (32.1%) and lower (67.9%) extremities. NT was used in the form of applications in combination with massage and therapeutic exercises.

The use of NT contributed to a positive therapeutic effect in 38 (79.7%) patients: a significant regression of motor and sensory disorders, an increase in the volume of active and passive movements was observed. NT had a pronounced analgesic effect (in 60.4% of cases). There was an increase in the amplitude of the M-response in the thenar and hypothenar muscles (p 0.001). The effect of NT on the conductive functions of peripheral nerves was less pronounced.

In patients with the injury of the nerves of the lower extremities after a course of NT, there was a decrease in the threshold of the H-reflex, the duration of the latent period, an increase in the amplitude of the M-potential from the medial gastrocnemius muscle from 2.3±0.3 to 3.8±0.2 mV (p <0.001).

RVG studies showed an increase in the rheowave amplitude (in the forearm - by 13.4%, in the lower leg - by 28.1%) and the rheographic index, which indicated an increase in the intensity of blood filling.

Conclusion: According to the study, NT has a positive effect on clinical and neurophysiological parameters in patients with GIPN. These factors justify the use of NT in the rehabilitation of patients with GIPN.

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Effect of mirror therapy on the recovery of upper limb function in individuals with chronic stroke: a systematic review

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Question: Is Mirror Therapy more effective than other interventions in the recovery of upper limb function in individuals with chronic stroke?

Background: Mirror therapy (MT) is used to improve motor function after stroke. During MT, a mirror is placed between the two upper limbs (UL), thus reflecting movements of the non- affected side as if it were the affected side.

Objectives: The aim of this review is to analyze the evidence on the effectiveness of MT in the recovery of UL function in population with post chronic stroke.

Methods: The literature search was carried out in PubMed, ISI Web of Science, and PEDro database. Inclusion criteria: a) studies that include individuals diagnosed with stroke for at least 6 months; b) intervention with MT in UL or comparing it with other interventions; c) articles published until 2023; d) articles published in English or Portuguese; e) randomized controlled studies. Exclusion criteria: a) animal studies; b) studies that do not provide a detailed description of the intervention; c) Studies using central electrical stimulation. Eighteen studies met all the inclusion criteria

Main results and conclusions: Results suggest that MT is more effective than other therapies in motor recovery and function of the affected UL, than these techniques alone, although the results have been modest in most of the included studies. There is also a more significant improvement in the distal movements of the affected hand than in the rest of the UL.

Keywords: Physical Therapy; Mirror therapy; Chronic stroke; Upper limb; Hemiplegia

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Use of JOGO EMG biofeedback in post op laminectomy L2-L3 with Cauda Equina Syndrome in improving gait and dynamic balance

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Background: Cauda Equina syndrome is treated with decompression by lumbar laminectomy. However, this procedure may develop certain musculoskeletal complications such as instability, bony regrowth, kyphosis, etc. We present a case with instability and functional difficulties post-laminectomy, which showed significant improvement with EMG biofeedback.

Case Report: A 62-year-old male driver with a history of chronic low back pain, was diagnosed with Cauda Equina Syndrome two years ago. He had a minor fall due to pain and weakness in his bilateral lower limbs and underwent posterior decompression of the L2-L3 vertebrae. Post-surgery, the patient complained of imbalance while standing and walking and was not able to do voluntary dorsiflexion of both ankles due to the tibialis anterior muscle weakness. He was started on JOGO EMG biofeedback therapy 12 sessions over 4 weeks along with static and dynamic balance and gait training, ADL training, coordination, and strengthening exercises. The patient showed improvement in the Functional Independence Measure from 37 to 57 out of 63, the Asia Impairment Scale from grade B to grade C, and manual muscle testing (left lower limb from 1 to 2; right lower limb from 2 to 3 out of 5), from 14 to 37 in the Berg Balance Scale out of 56. EMG peak potential amplitude increased from 5–12 mVs to 14–23 mVs.

Conclusion: JOGO EMG biofeedback therapy provided real-time feedback on muscle activity, which in turn facilitated the activation of tibialis anterior muscle. There was increase in the patient's muscle activity and his ability to perform basic activities improved. His gait and dynamic balance also improved significantly.

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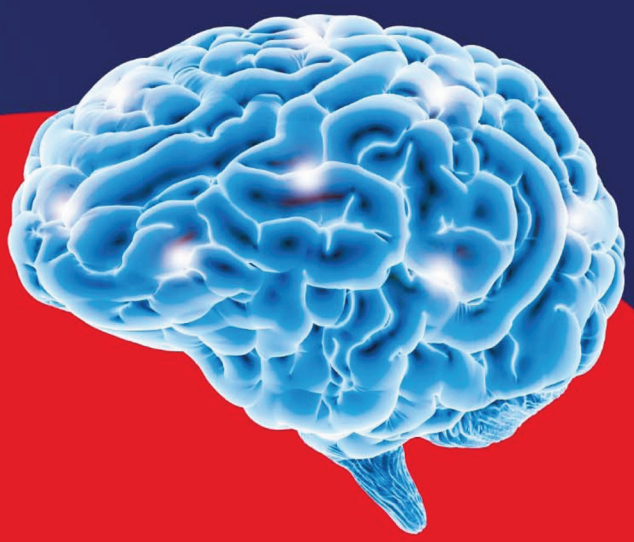
Sleep



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Sex differences in associations between sleep state-specific apnea severity and symptoms of depression among patients with obstructive sleep apnea

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Objective: There is a high prevalence of depression in patients of obstructive sleep apnea (OSA). However, an association between depression and OSA severity is unclear. Recent studies found that increased OSA severity is associated with less depression and anxiety. Therefore, we aimed to investigate 1) whether such possible associations differ depending on sex and 2) which of apnea severities during REM and NREM sleep is more likely associated with depression and anxiety.

Methods: Symptoms of depression and anxiety were defined as a Patient Health Questionnaire-9 score ≥10 and a Generalized Anxiety Disorder-7 score ≥8, respectively. Apnea severity was categorized using the conventional cutoffs of apnea-hypopnea index. Logistic regression analyses were conducted.

Results: We included 1,346 adult OSA patients (80.2% men). Symptoms of depression and anxiety were present in 14.8% and 14.4% of patients, respectively. Severe OSA was significantly less likely than mild OSA to be associated with the presence of depression and anxiety after controlling for age, sex, daytime sleepiness, diabetes, and medical comorbidities. Such negative associations were found in men, but not in women. When both apnea severities during NREM and REM sleep were entered into the same logistic regression model, severe OSA during NREM sleep, but not during REM sleep, was associated with less depression and anxiety in adjusted models. Such relationships were also significant in men, but not in women.

Conclusions: Increased apnea severity was associated with less depression and anxiety, but only in men. Such negative associations were evident when using apnea severity during NREM sleep.

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Does Periodic limb movements during sleep (PLMS) not require treatment? The relationship between PLMS and insomnia, obesity and arrhythmia

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Objectives: Periodic limb movements during sleep(PLMS) is generally known to accompany restless leg syndrome(RLS), and there is not much research on PLMS itself. Moreover, the relationship between insomnia and PLMS is underrecognized. This study aimed to investigate the polysomnography (PSG) data, questionnaires, and iron-related laboratory data of patients who visited Insomnia and were confirmed PLMS.

Methods: Between 2015 and 2022, 423 patients with insomnia as the primary symptom who diagnosed periodic limb movements in overnight PSG were included. Patients were divided into three groups based on their PLM index (PLMI). The participants' demographics, insomnia related questionnaires, PSG findings, and iron-related laboratory findings were used in the analysis.

Results: Severe PLMS group (PLMI 50) were mostly males, had more people taking sleeping pills and had higher body mass index (BMI) than mild PLMS group(PLMI 5-25). Significant differences were not found in questionnaire about insomnia and sleep quality. In PSG, severe PLMS group showed shorter total sleep time and low spontaneous arousal index than mild to moderate PLMS groups. And more patients in the severe PLMS group were showed arrhythmia than mild PLMS group. Ferritin, transferrin saturation results were not different between groups.

Conclusions: PLMS did not affect the severity of Insomnia or fatigue during daily life. The results shown in PSG may be influenced by age or taking sleeping pills. The most significant result was that arrhythmia was higher in the severe PLMS group. More research is needed on the causal relationship between PLM and cardiac diseases.

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Sleep in Clinical Populations of Neurodegenerative Disorders

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Neurodegenerative diseases, including Alzheimer's Disease, Parkinson's Disease, and Lewy Body Dementia, are often associated with sleep/wake disturbances. However, the specific patterns and mechanisms underlying these disturbances remain unclear. This presentation will highlight the different patterns of sleep-wake phenotype associated with different neurodegenerative disorders, namely Alzheimer's Disease (AD), Progressive supranuclear palsy (PSP), Corticobasal syndrome, Parkinson's Disease, and Dementia with Lewy Body. Of particular interest is the role that hyperarousal and disturbed sleep have in the production and clearance of proteins implicated in neurodegeneration. The presentation will also highlight the importance of considering focal and network issues related to the spread of pathologic proteins and site-specific vulnerability across proteinopathies which may account for different sleep phenotypes being linked to different neurodegenerative disorders.

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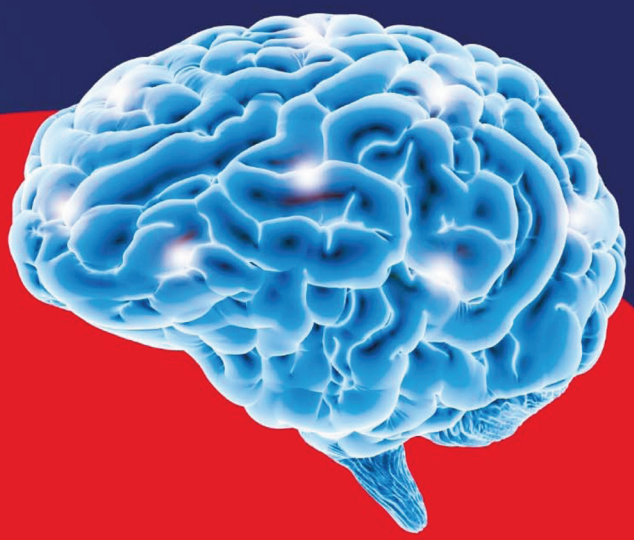
Stroke



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Isolated weakness of the index finger flexion in subcortical infarction

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The efferent projections from the cortical area of the hand have not been fully defined. Moreover isolated finger weakness in association with cerebral infarction is rare. A 60-year-old man suddenly developed weakness in his left index finger. MRI clearly demonstrated that a discrete infarction was the cause of weakness of isolated index finger flexion in this patient. The lesion was located in the medial margin of an inverted omega-shaped precentral knob on axial MRI and in the subcortex of right frontal lobe on coronal MRI. Currently, there has been a controversial debate in the neuroscience community as to whether or not finger somatotopy in the primary motor cortex exists. Several studies on stroke patients supported the existence of alleged topography for fingers in the human motor cortex: ulnar fingers–medial and radial fingers–lateral. Other investigators demonstrated multiple representation or spatially overlapping patterns of the cortical motor hand area. Unexpectedly, the MRI lesion does not agree with a previous report that predominant weakness of radial- sided fingers is usually caused by laterally located infarcts whereas weakness of ulnar fingers is related to medial lesions in the precentral knob, topography, which also was observed in the previous report. Despite this, observations in my patient may be of value because this is the rare report of isolated index finger flexion weakness caused by a small subcortical infarction. At the least, this findings strongly suggest that a discrete area for index finger flexion may exist.

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ABCG2 Gene Polymorphisms May Affect the Bleeding Risk in Patients on Apixaban and Rivaroxaban

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Direct oral anticoagulants (DOACs) are widely used for stroke prevention in atrial fibrillation. However, they have a bleeding complication. Breast cancer resistance protein, encoded by ABCG2, is known to be an efflux transporter of apixaban and rivaroxaban among DOACs. This study investigated the association between gene variants and bleeding complications during treatment with ABCG2 substrates (apixaban and rivaroxaban). Patients treated with apixaban and rivaroxaban were enrolled from June 2018 to December 2021. Five single nucleotide polymorphisms (SNPs) of ABCG2 were selected. Previously studied genes (ABCB1, CYP3A4, and CYP3A5) were further analyzed as possible confounders. Finally, a total of 16 SNPs were examined in this case–control study. The outcome was defined as major bleeding and clinically relevant non-major bleeding. Among 293 patients, 64 were cases. The mean age of the patients was 68.8 years, and males were 62.5%. Multivariable Model I revealed that a history of bleeding, concurrent use of proton pump inhibitor (PPI), ABCG2 rs3114018, and ABCB1 rs1045642 were significantly associated with bleeding complications; the AORs (95% CI) were 6.209 (2.210–17.442), 2.385 (1.064–5.349), 2.188 (1.156–4.142), and 3.243 (1.371–7.671), respectively. Model II showed that modified HAS-BLED score, concurrent use of PPI, ABCG2 rs3114018, and ABCB1 rs1045642 were significantly associated with bleeding complications. In conclusion, the modified HAS-BLED score, a history of bleeding, concurrent use of PPI, ABCG2 rs3114018, and ABCB1 rs1045642 were significantly associated with the risk of bleeding complications in patients on apixaban and rivaroxaban, after adjusting for other confounders.

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Acute multifocal cerebral microhemorrhages in patient with chronic pancytopenia

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Cerebral microhemorrhages are small sized, focal, perivascular hemosiderin depositions and known to occur well when there are risk factors such as chronic hypertension and brain amyloid vasculopathy. There lesions are well detected by Gradient echo MRI and susceptibility weighted imaging sequences. We report a case of sudden onset multifocal cere-

bral microhemorrhages in patient with chronic pancytopenia.

A 77-year-old man visited due to general weakness and fever. Blood tests confirmed platelets 21,000/μL, fibrinogen 582 mg/dl, D-dimer 3.70 mg/L, prothrombin time 31.0 seconds. Klebsiella pneumoniae was identified in blood culture tests and IV ceftriaxone was started. After that, petechia occurred throughout the body. On neurological examinations, mental status was drowsy and brainstem reflexes were normal. The muscle strength represented MRC motor grade 4. Sensory tests and cerebellar function tests were not performed due to poor cooperation. Deep tendon reflexes reduced without asymmetry in all extremities. Babinski reflex showed negative responses. Multiple microhemorrahges were found in the entire brain on imaging.

In addition to the various conditions mentioned earlier, as a secondary result of hypoxia accompanied by severe diseases or bacterial or viral infections, vascular endothelial dysfunction may occur, and ultimately red blood cells may leak out of the blood vessels inside the brain, resulting in microhemorrhages in the brain. In this case, it is estimated that a wide range of acute cerebral microhemorrhages occurred due to microthrombosis in blood vessels and hemoglobin deposits around small blood vessels after the occurrence of disseminated intravascular coagulation due to severe infection with chronic pancytopenia.

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The global trends of neuronal autophagy in ischemic stroke from 2005 to 2022 by bibliometric analysis

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Objective: Autophagy, one of the mechanisms that determine the ultimate fate of different cell types. The balance between the burden of intracellular substrate targeted for autophagy and the capability of the cellular autophagic machinery regulates whether autophagy is useful or harmful in ischemic stroke (IS). Neuronal autophagy plays a double-edged sword role in IS.

Method: This retrospective observational bibliometric study was collected from 2006, through March, 2022. We visually analyzed the research hotspots of neuronal autophagy related to IS, and generated various visual maps to display publications, authors, sources, countries, organizations, and keywords.

Result: A systematic search was conducted and yielded 242 articles. Since 2006, the role of neuronal autophagy in IS has received widespread attention and gradually become a hot topic in this context. Many institutions and authors made outstanding contributions to this field. The majority of institutions were from China and the United States. We discovered that investigations of autophagy in IS have focused on both brain injury and neuroprotection. Neuronal autophagy after IS is widely related to a variety of signaling pathways and inflammatory factors. Autophagy plays an important role in all phases of IS.

Conclusions: The effect of neuronal autophagy on IS will continue to become a hot topic, which is of great significance in guiding the development of new therapy for IS. Autophagy-related pathways will become the focus of future research. Regulation of neuronal autophagy at different stages after IS may reduce neuronal injury and promote nerve repair and even regeneration.

Keywords: Neuron; Autophagy; Ischemic Stroke; Bibliometric analysis; Web of Science

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The CT collateral map: Assessment of baseline lesion and penumbra after Acute Ischemic Stroke

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Background and purpose: The MR collateral has demonstrated prognostic value in functional and tissue outcomes of patients with acute ischemic stroke (AIS). We investigate whether the CT collateral map can assess the baseline lesion and penumbra.

Materials and Methods: We generated CT collateral maps derived from CT perfusion, which comprised images of arterial, capillary (CMC), early venous (CMEV), late venous, and delay phases. Volumes of DWI lesions, CBF 30%, Tmax 6 s, and hypoperfused lesions on CMC and CMEV in baseline imaging and follow-up DWI lesions were measured. The concordance correlation coefficients of the volumes of CBF 30% and hypoperfused lesions on CMEV for the volumes of baseline DWI lesions were analyzed. In patients with unchanged arterial lesions on follow-up angiography, the concordance correlation coefficients of the volumes of Tmax 6 s and hypoperfused lesions on CMC for the volumes of follow-up DWI lesions were analyzed.

Results: One-hundred eleven patients (mean age ± standard deviation, 71.6 ± 13.7; 60 women) were included. The concordance correlation coefficients the volumes of CBF 30% and hypoperfused lesions on CMEV for the volumes of baseline DWI lesions were 0.76 (95% CI, 0.60-0.91) and 0.97 (95% CI, 0.95-0.98), respectively. The concordance correlation coefficients of the volumes of Tmax 6 s and hypoperfused lesions on CMC for the volumes of follow-up DWI lesions were 0.12 (95%CI, -0.03-0.56) and 0.97 (95% CI, 0.93-0.99), respectively.

Conclusions: Precise prediction of the baseline lesion and penumbra can be possible using the CT collateral map.

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Isolated weakness of middle, ring, and little fingers due to a small cortical infarction in the medial precentral gyrus

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Background: Small cortical strokes can produce predominant isolated weakness in a particular group of fingers: radial or ulnar. The traditional views are of point-to-point representations of each finger to neurons located in the precentral gyrus of the motor cortex such that the neurons of the radial fingers are located laterally and those of the ulnar fingers are located medially. We present a case of isolated weakness of middle, ring, little fingers due to small cortical infarction in lateral precentral gyrus with functional MRI.

Case: A 58-year-old man suddenly developed weakness in his right middle, ring, little fingers. On examination, motor examination revealed mild weakness (IV) of his right middle, ring, little fingers. The weakness was most severe at the distal interphalangeal joint. The power of finger flexion and extension are equally affected.

Conclusion: In spite of our patient had predominant ulnar-sided finger weakness, the location of the lesion was more lateral side in precentral gyrus. We found the correlation between diffusion weighted MRI lesion and functional MRI lesion in our patient.

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The protective effect of hydroxylsafflower yellow A on neurons after OGD/R based on autophagy and pyroptosis

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Objective: To investigate the protective effect of hydroxysafflower Yellow A (HSYA) on neurons after Oxygen-glucose deprivation/reoxygenation (OGD/R) injury by regulating autophagy and pyroptosis.

Methods: HT22 cells at the logarithmic growth stage were randomly divided into 4 groups: normal group, model group, HSYA group, and rapamycin group. Except normal group, the cells in other groups were treated with hypoxia and glucose deprivation for 2h and reoxygenation and glucose restoration for 24h. Cell activity was detected by the CCK-8 method, cell damage was detected by the LDH method, protein expression of LC3 and NLRP3 were observed by immunofluorescence staining, and protein expression of LC3, p62, NLRP3, Cleaved Caspase-1, GSDMD, and IL-1β were detected by Western blot method.

Results: Compared with the normal group, the cell viability and LDH leakage rate in the model group were significantly decreased. Immunofluorescence results showed that the protein expressions of LC3 and NLRP3 were increased. Western blot results showed that the intracellular expressions of LC3-II/LC3-I were increased, the expression of p62 was decreased, and the protein expressions of NLRP3, Cleaved Caspase-1, GSDMD, and IL-1β were significantly increased. After the intervention of HSYA and rapamycin, the ratio of LC3-II/LC3-I increased, and the expression of p62 and pyrodeath-related proteins decreased compared with the model group.

Conclusion: HSYA can improve the neuronal survival rate after OGD/R, which may be related to promoting autophagy and inhibiting pyroptosis induced by NLRP3 inflammasome.

Keywords: Pyroptosis; Autophagy; Hydroxysafflor yellow A; Neurons; Oxygen-glucose deprivation/reoxygenation (OGD/R)

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Clinical and Neirovisual correlation in Patients with post Stroke depression

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Post Stroke depression is an interesting and common occurrence. Depression is one of the major impediments to full physical and mental recovery from stroke,

We observed 40 patients during the last year (after post pandemic period) period with post stroke depression. In 75% (30 cases) stroke was ischemic and in 25% (10 cases) -hemorrhagic. In 50% (24 cases) post stroke depression was developed within the first one to two months after the stroke, in 25% (10 cases) post stroke depression was developed during the first 6 months after the stroke, in 13.3% (5 cases) with hemorrhagic stroke, depression was developed after years, 10% (4 cases) after month and in one case (1.7%) after two days. All cases of stroke, were

established by CT and MRI investigations and pathological processes mainly observed in Frontal and Frontal-Occipital area. All patients were reviewed according Hospital Anxiety and Depression Scale (HADS).

Post stroke depression is most often treated with antidepressant medications. We used antidepressants in a group of patients aged 60 to 80 years: Alprazolam, Citalopram and Alprazolam at the same time and Sertraline.

Although Alprazolam showed the best results our study did not revealed relative effectiveness of one of the drugs used in the patients and also no difference was found due to the type of the disease (ischemic or hemorrhagic).

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Case report: A patient with ischemic stroke and epileptic status

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Symptoms in ischemic stroke and those during and after an epileptic seizure can be a differential diagnosis problem. These two conditions, though rarely, can manifest at the same time in the same patient. It is important that they are quickly demarcated in order to treat the different etiologal and pathogenetical mechanisms accordingly.

Here we present the case of a 56 year old male with history of epilepsy, which during a routine EEG develops acute left side limb weakness. CT of the brain showed no signs of acute ischemic stroke or hemorrhage, so treatment with Actilyse was started. The immediate reaction of the medical team in assessing the condition and the treatment that followed are the reasons the patient managed to overcome the neurologic deficit.

A multidisciplinary team was formed during the patient's stay in order to assess the different complications that arose, such as pneumonia and pleural effusion, difficulty breathing and consciousness disturbances.

Along with all the medications administered, repetitive transcranial magnetic stimulation was performed in order to activate the brain's neuroplasticity mechanisms that help speed up the recovery process.

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Efficacy and Safety of Injection Tenecteplase in 4.5 to 24 hours imaging eligible window patients with Acute Ischemic Stroke (EAST-AIS) – An Interim analysis

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Background and Aims: Current practice of intravenous thrombolysis for Acute Ischemic Stroke (AIS) patients approved within window period of 0-4.5 hours. This study evaluates the efficacy and safety of injection Tenecteplase in AIS patients within extended window period of 4.5-24 hours from onset.

Methodology: This randomized controlled trial is being conducted at a tertiary care hospital after Institute Ethics Committee approval with CTRI registeration- CTRI/2022/03/040718. A total of 100 patients shall be randomized in our trial. Injection Tenecteplase (0.25 mg/kg bodyweight; maximum 25 mg) will be administered to 50 patients and 50 patients will be administered similar looking placebo. A total of 24 patients have been randomized; first patient was enrolled on 1st August, 2022.

Results: Interim analysis of adverse events was carried out with ten included patients. 70% (7/10) were males, 51.1 years was the mean age of presentation and 431 minutes (7 hours 18 minutes) was the average time of onset. Symptomatic intracerebral-hemorrhage was observed in two patients in active trial drug group and in one patient in placebo group. Out of 10 patients, decompressive hemicraniectomy was observed in three patients in active trial drug group and two in placebo group. One patient of active trial drug group and in two patients of placebo group observed infarct growth. Out of 10 cases; three deaths were observed.

Conclusion: This is an ongoing trial, with 76 eligible patients yet to be enrolled. The results of this trial may give us information regarding future management of ischemic stroke in extended window-period.

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Predicting Contrast Induced Acute Kidney Injury Risk in Acute Basilar Artery Occlusion: Combination of Pre-Procedural Systemic Inflammation Response Index and D-Dimer to Fibrinogen Ratio

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Background: Discussing the predictive value of pre-procedural Systemic Inflammatory Response Index (SIRI) combine with D-dimer to fibrinogen ratio (DFR) for Contrast Induced Acute Kidney Injury (CI-AKI) in patients with Acute Basilar Artery Occlusion (ABAO) underwent thrombectomy.

Methods: Clinical data were collected from January 2019 to March 2023. Patients were divided into CI-AKI group (23) and Non-CI-AKI group (90), based on the occurrence of CI-AKI after thrombectomy. Logistic regression was used to analyze the risk factors for the occurrence of CI-AKI. The Restricted Cubic Spline (RCS) was used to model the correlation between SIRI, DFR, and CI-AKI. The Receiver Operating Characteristic (ROC) curve was drawn to evaluate the predictive value of SIRI, DFR and their combined indicators for CI AKI.

Results: The incidence of CI-AKI was 20.4% (23/113). Multivariate logistic regression analysis demonstrated that ln (SIRI) (OR=2.020, 95% CI: 1.076-3.791; P=0.029) and ln (DFR) (OR=1.549, 95% CI: 1.043-2.301; P=0.030) were independent influencing factors for CI-AKI in ABAO patients post-thrombectomy. RCS analysis showed that when SIRI 2.67 and DFR 0.18, there was a significant positive correlation with the occurrence of CI-AKI. In receiver operating characteristic analysis, the area under the curve for SIRI combined DFR was 0.729 (95% CI: 0.610-0.848; P = 0.001).

Conclusion: An increase in SIRI and DFR within certain ranges can effectively predict the risk of CI-AKI occurrence in ABAO patients underwent thrombectomy, and the combined prediction of the two has greater significance.

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Clinical profile and outcomes of Cerebral Venous Sinus Thrombosis in a Tertiary Care Setting in Sri Lanka

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Background and Aims: Cerebral venous sinus thrombosis (CVST) is rare form of stroke. Etiology of CVST is broad. This study aims to analyze clinical and radiological profile of CVST in Sri Lanka.

Methodology: An observational prospective study included 28 adult participants with symptomatic CVST. They were assessed at diagnosis, 6 months and 1 year.

Results: Median age of the population was 35 years with female majority (82.1%, n=23). Commonest symptoms were headache at 89.3% (n=25), seizures and focal neurological deficits (42.9%, n=12 each). Commonest risk factors were oral contraceptive use in 25% (n= 7), local infections in 14.7 and APLS in 10.7%. Radiological features consist of Sinus hyperdensitiy in 28.6% (n=8), cerebral edema and empty delta sign at 14.3% each (n=4).42.9% (n=12) had single venous sinus involved. Commonest sinuses to be involved were superior sagittal and Transverse sinuses in 53.6% (n=15) each. Venous infarcts and hemorrhages accounted for 78.6 % (n=14). Isolated intracranial hypertension was detected in 32.1% (n=9), Visual loss in 10.7 (n =3), recurrent CVST and arterio-venous fistulas in 7.1% (n=2) each. All patients received anticoagulation. Majority (96.4%,n=27) recovered. During follow up magnetic resonance scanning, partial recanalization of sinuses was evident on 21.4% (n=6).

Discussion: Sri Lankan Profile of CVST is mostly similar to regional and international studies, although had high-rate local infections and hypercoagulable state. Pregnancy was less in number. Increased frequency of Isolated intracranial hypertension was detected. Comparatively, long-term vi-

sual complications were high. Majority had good outcome from CVST.

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Baicalin prevents cerebral ischemia-induced neurobehavioral disorders and brain damage

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Cerebral ischemia is known that causes neurological disorder, neuronal cell death, and permanent disability. Baicalin has antioxidant and anti-apoptotic properties. The aim of this study was to investigate the neuroprotective effect of baicalin in animal models of stroke. Middle cerebral artery occlusion (MCAO) was performed to induce focal cerebral ischemia and baicalin (30 mg/kg) or vehicle was injected intraperitoneally just before MCAO surgery. Neurological behavior tests including neurobehavioral scores, corner test, adhesive removal test, and vibrissae evoked forelimb placing test were performed 24 h after MCAO. Brain edema and infarct volume were measured. To investigate the antioxidant effect of baicalin, reactive oxygen species (ROS) and lipid peroxidation (LPO) levels were measured. Hematoxylin and eosin staining and terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) histochemical staining were performed. There were significant neurobehavioral defects in MCAO-treated animals. However, in the presence of baicalin, neurobehavioral defects due to MCAO surgery were significantly attenuated. MCAO damage causes severe cerebral edema and increases infarct volume, and baicalin treatment alleviates these changes caused by MCAO. The cerebral cortex of MCAO animals showed histopathological changes with condensed nuclei and expanded cytoplasm and increased TUNEL positive responses. However, administration of baicalin attenuated histological lesions caused by MCAO. In addition, baicalin treatment alleviated MCAO-induced increases in ROS and LPO levels. We showed that MCAO damage caused severe neurobehavioral impairment and brain tissue damage, and baicalin exerted neuroprotective effects by regulating apoptosis and oxidative stress. Therefore, these results suggest that baicalin acts as a neuroprotective agent in stroke animal models.

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Functional Outcomes of Ischemic Stroke in Patients Treated with Mechanical Thrombectomy in Grodno, Belarus

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Background: Mechanical thrombectomy (MTE) for large vessel occlusion in ischemic stroke has proven to be effective in large clinical trials.

Objective: To establish the functional outcomes of ischemic stroke in patients treated with MTE in the clinical routine.

Methods: The subjects of the study were 30 ischemic stroke patients treated with MTE in 2021–2022 at the Grodno University Hospital. The primary endpoint was the modified Rankin Scale (mRS) score 3 months after stroke onset.

Results: The median age of patients was 64 years (interquartile range (IQR) 59–69) and the median NIHSS score at admission was 16 (IQR 12–19). 17 patients (57%) had occlusion of the M1 segment of the middle cerebral artery, 6 patients (20%) had occlusion of the M2 segment, and 7 patients (23%) had occlusion of the internal carotid artery. In 14 patients (47%), thrombolysis was performed before thrombectomy. After MTE, 20 patients (67%) had level 2b/3 on the mTICI scale. The median NIH score at 24 hours decreased to 14 (IQR 10–18). Within 7 days from the onset of stroke, the median NIH score decreased to 12.5 (IQR 6–18). 27% of patients (8/30) 3 months after the onset of stroke were functionally independent in daily life (mRS 0–2), 43% (13/30) had signs of disability (mRS 3–5). The 90-day mortality rate was 30% (9/30).

Conclusions: Functional outcome was less favorable and higher mortality rates were observed than reported by authors of large randomized trials, likely due to less stringent inclusion criteria.

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Prospective and Retrospective Study of Tenecteplase at Single Tertiary Center in Western India

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Ischemic stroke is a brain attack caused by a sudden interruption in the blood supply of the brain. Approximately two million brain cells destroy every minute during a stroke. This increases the risk of brain damage, disability and death. In India there are 145-154 strokes per 100,000 population yearly. About 185,000 strokes occur every year. One stroke occurs every 40 seconds. Stroke is the fourth leading cause of death and one stroke death occurs every 4 minutes. Thrombolytic treatment is the most promising treatment for acute ischemic stroke. Initiation of treatment within the window period 4.5 hrs. with a clot dissolving drug restores the normal blood flow. The drug works by splitting plasminogen into plasmin leading to fibrin degradation. Tenecteplase has more fibrin specificity and a longer half-life. It is much cheaper than Alteplase and very easy to administer. This study shows the efficacy, safety and cost effectiveness in a country like India. There are very few studies conducted in India showing the safety and efficacy of Tenecteplase (TNK). We prospectively and retrospectively studied the efficacy, symptom resolution and safety outcomes of TNK in 100 adult patients with acute ischemic stroke. Patients coming in the window period (4.5 hours) or wake up stroke with Flair Diffusion Mismatch on MRI were studied. The efficacy outcome measures included improvement in NIHSS score, Modified Rankin score and GCS score at 24hr, on discharge and at 90 days. In our study we also analyzed post thrombolysis intracranial hemorrhage (ICH), symptomatic ICH, morbidity and mortality within 90-days.

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Charles Bonnet Syndrome as Sequelae of Occipital Lobe Infarct With Hemorrhagic Conversion: A Case Report

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Charles Bonnet syndrome occurs in the setting of visual impairment with subsequent complex and repetitive visual hallucinations confined in the area of visual loss, with intact cognition and insight. It has been described as a sequelae of ischemic stroke affecting the visual pathway. We report a case of a male presenting with right homonymous hemianopsia secondary to acute left occipital lobe infarct of cardioembolic etiology. He then developed visual hallucinations on the side of the visual loss. MRI showed hemorrhagic conversion of the occipital lobe infarct. Electroencephalogram showed focal and intermittent slowing of the anterior temporal and frontal region. Charles Bonnet syndrome may signify the worsening or progression of a structural lesion affecting the visual pathway, such as hemorrhagic conversion, and warrants prompt and thorough evaluation. Understanding these conditions is crucial for healthcare professionals and caregivers to provide effective support and interventions for those affected.

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Muscle Measures of Acute Deconditioning after Stroke

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Background and aims: Stroke-related sarcopaenia is a recognised complication of stroke that contributes to poor prognosis. Estimates suggest over a third of stroke survivors are sarcopaenic at 6 months, however, little existing data inform us how quickly such changes to muscle occur.

Methods: This single-centre, longitudinal observational study recruited individuals admitted within the first week of stroke (Sheffield, UK). Socio-demographic and clinical details were recorded, alongside weekly assessment of mid-femoral circumference (MFC), mid-humeral circumference (MHC), and bioelectrical impedance analysis (BIA). Appendicular skeletal muscle mass (ASM) was estimated from validated formulae (European Working

Group on Sarcopaenia in Older People) and muscle strength using unaffected handgrip strength (HGS, Kg). Weekly assessments continued until discharge from hospital. Wilcoxon Signed Rank tests and one-way ANOVA were then used to investigate timings and significance of these changes accordingly.

Results: 30 participants were enrolled, mean (SD) age 72.7 (11.5) years, 59% female, mean (SD) NIHSS 9.5 (6.0), average length of inpatient stay 28.2 days. Statistically significant reductions in affected and non-affected limb MFC (-1.03 cm,p=0.039; -1.14cm,p=0.003 respectively), affected limb MHC (- 0.81cm,p=0.021) and ASM (-0.7kg,p=0.028) were observed, while non-affected MHC and HGS were unaffected. Within the first 2 weeks non-affected MFC reduced by 2.1% (p= 0.012) and ASM 6.0% (p= 0.277).

Conclusions: Significant changes to muscle mass can be detected within the first 2 weeks of stroke, suggesting physiological muscle changes occur before this time. Potential interventions mitigating muscle loss may need to be initiated in the hyperacute period after stroke in order to be effective.

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Elevated NR2AB NMDA Receptor Levels in Patients with Chronic Cerebral Ischemia may be a Predictor of Cerebral Vascular Accident

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Introduction: It is known that the detection of NMDA receptor NR2-antibodies (NR2ab) in the blood of stroke patients is highly sensitive to ischemic damage than to hemorrhagic. Arterial hypertension (HP) is a major risk factor for stroke and also leads to cerebral white matter damage long before cerebral infarction. In this study, we aimed to evaluate the level of NR2ab in patients with chronic cerebral ischemia (CCI) and HP.

Materials and Methods: The study included 52 patients with CCI and HP who had never previously suffered an acute ischemic stroke (AIS) in their lives. Exclusion criteria: no history of ischemic or hemorrhagic stroke, any neurodegenerative, neuroinflammatory, and psychiatric diseases. The study participants were observed by a neurologist, underwent baseline examinations according to the protocol and brain MRI (1.5 Tesla), where brain matter lesions were verified on the Fazekas scale of grade 2. Patients underwent routine venous blood sampling and serum NR2ab levels were determined using the NR2AT-ELISA Human Kit (DRD Biotech).

Results: The mean NR2Ab values show 1.42ng/ml (range, 0.51-3.64, 95% CI: 1.2-1.6), a mean age of 55.71±1,642 years (95% CI: 52.41-59.01). Patients, who suffered more severe CCI symptoms and their combinations, had the higher level of NR2Ab. Neurological examinations revealed memory problems, imbalance while walking, difficulties performing two or more tasks simultaneously, mood swings, and depression in such patients (the HADS and the MOCA scales were used). Three patients showed the highest NR2ab levels: 2.9, 2.98, and 3.64 ng/ml, and during 1-2 days they developed a transient ischemic attack.

Conclusion: Elevated NR2ab levels in patients with CCI (Fazekas grade 2) + HP may be considered as a biomarker predicting vascular catastrophe, further studies are required.

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Cilastazole in secondary prevention of recurrent stroke

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Introduction: Recurrent stroke has major clinical and social morbidities. Search for a better treatment option to mitigate the risk of stroke recurrence with

least possible adverse effects has encouraged many studies to assess the benefits of various anti-platelet therapies either alone or in combination. Aspirin and clopidogrel or ticagrelor dual therapy has been proven to be beneficial in preventing stroke recurrence but increases the risk of major bleeding complications beyond a month. Cilastazole a phosphodiesterase (PDE 3) inhibitor showed promising effects in peripheral arterial diseases, with minimal adverse events. This is a case series of recurrent non-cardioembolic strokes, who were initiated on Cilastazole based dual antiplatelet therapy, to compare the long-term stroke outcome and tolerance.

Methodology: Data of patients visiting neurology OPD for regular follow up with prior history of recurrent non-cardioembolic stroke was collected. Those with recurrence due to medication non-compliance and uncontrolled vascular risk factors or concurrent cardiac events were excluded. Those patients who were treated with a dual anti-platelet therapy with Cilastazole and either aspirin or clopidogrel were analyzed. These patients were followed up for at least one year.

Results: 12 patients with mean age of 63.3years (50-72yrs) were started on Cilastazole after recurrence on initial antiplatelet therapy. They were followed up over a mean of 3.9 years (1-3 yrs). One had recurrence while on CLZ(8%). None reported any events of major bleeding or systemic complications requiring to stop or alter the medication.

Conclusion: Cilastazole appears promising in prevention of recurrent stroke, with least risk of intracranial bleed. Further studies are needed to confirm the results.

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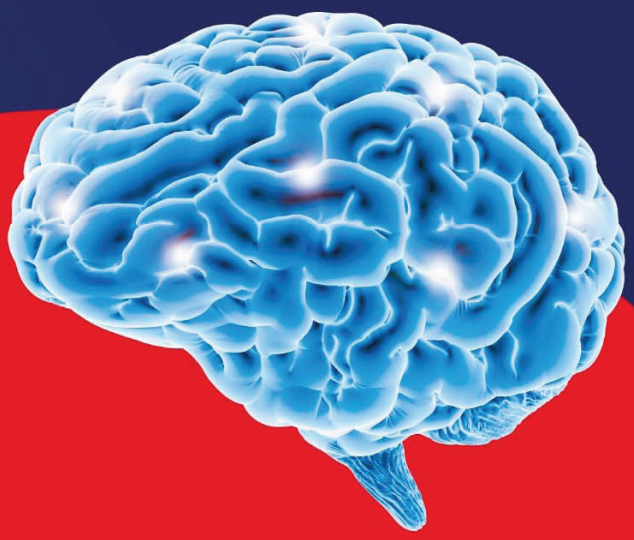

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Identifying Sensitive Neuropsychological Tests for Cognitive Decline in Highly Educated Older Adults: A 10-Year Longitudinal Study

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Background: Timely detection of cognitive decline in highly educated adults is challenging due to their resilient cognitive abilities, and limited sensitivity of neuropsychological tests for this group. Therefore, evaluating subjective facets, such as subjective cognitive decline (SCD) becomes imperative, as it may facilitate early identification of cognitive decline in this group.

Objective: Our primary objective was to identify effective methods, both objective and subjective, for early detection of cognitive decline in highly educated older adults, over a decade. We sought to explore the associations between objective cognitive decline with SCD, depression, and anxiety while presenting a Hebrew SCD questionnaire.

Methods: Initially, the study included 28 highly educated participants (13 men and 15 women, ages 66 to 80, 12 to 24 years of education). At T7 (final year), 20 participants were included (10 men and 10 women, ages 74 to 89). Assessments comprised comprehensive evaluation including cognitive tests and questionnaires assessing depression, anxiety, and SCD.

Results: Significant declines were observed in tests based heavily on executive functions, specifically in the Rey–Osterrieth Complex Figure Test (ROCFT) copy, $F(3,57) = 9.05$, p 0.001, $p2 = 0.32$, and Rey Auditory Verbal Learning Test (RAVLT) trial six, $F(1,19) = 7.32$, p 0.05, $\eta p2 = 0.28$. The Hebrew SCD questionnaire demonstrated high reliability and validity, highly correlated with cognitive decline.

Conclusions: Objective methods were more sensitive than subjective approaches in detecting cognitive decline, especially the ROCFT copy. However, the SCD questionnaire displayed predictive capabilities and should be further validated in future research.

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A threat forgotten in vain: the contemporary neurosyphilis encounter

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Introduction: The neurosyphilis can occur at any time after infection. Diagnosis is complicated by periods of active disease and latency. Neurosyphilis remains underdiagnosed, especially in cases of no history of diagnosed syphilis.

Methods: Case Report.

Results: 56yo man was admitted with ataxia, slurred speech, poor memory for 3-3.5 years and two recent Jacksonian seizures. He became apathetic, with poorly controlled urination.

2y earlier he was treated for subacute headache, disorientation, ataxia, and dysarthria. At that time general blood analyses, and rheumatologic and metabolic panel were normal; serum HIV, syphilis, and hepatitis were negative; CSF showed 12 lymphocytes/mL, protein 0.99 g/L with negative virology; brain MRI showed internal hydrocephalus and signs of cortical encephalitis.

In current admission patient had intelligence and memory decline, dysarthria, left central hemiparesis and ataxia. MRI demonstrated residual signs of previous inflammation and brain atrophy.

Blood analyses were unremarkable, except positive Lyme serology. Serum RPR test, Enzyme immunoassay (EIA) of serum and CSF were also positive. CSF cytosis and protein were normal.

Late neurosyphilis was confirmed. Positive Lyme tests were considered cross-reactive.

6 months after the start of the antibiotic treatment, patient's cognition improved, he started to control urination. He still had dysarthria and ataxia but was

able to walk and perform basic self-care activities and was free of seizures.

Conclusions: In cases of unspecified CNS disease, neurosyphilis should be examined as there might be latent forms. Early detection and appropriate treatment can prevent the permanent neurological deficit.

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Neuromuscular complications of COVID-19

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The aim of the study was to identify complications of COVID-19 infection in patients with neuromuscular diseases.

20 patients with myasthenia gravis, 8 patients with chronic polyneuropathy and 5 patients with progressive muscular dystrophy infected with SARS-COV-2 were examined. There were 15 women and 5 men among patients with myasthenia, age - 50-69 years, among patients with chronic polyneuropathy - 3 women, 5 men, age 25-74 years; There were 3 women and 2 men, aged 36-73 years, among patients with progressive muscular dystrophy. Patients were examined within a time interval of 3 weeks to 2 months after confirmed COVID-19 infection.

In 15 patients out of 20 with myasthenia gravis, an exacerbation of the condition was noted, of which Lambert-Eaton syndrome was diagnosed in one patient after COVID-19 and in 3 had motor-sensory polyneuropathy. Out of 8 patients with chronic polyneuropathy infected with COVID-19, the course of the disease worsened - in 4, of which one had clinical, electromyographic and biological markers characteristic of polymyositis. 40% of patients were diagnosed with axonopathy and demyelination of n. phrenicus. Of the 5 patients with progressive muscular dystrophy, 2 had sensory-motor polyneuropathy, which was not detected before infection, 1 patient had ENMG changes characteristic of polymyositis.

Based on the results obtained, it can be assumed that not only comorbid pathology occurs as a result of infection with COVID-19, but the COVID-19 virus can also be considered as a modifying factor in the course of the disease.

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Effect of Continuation of Intensive Phase on Poor Responders of Antituberculosis Treatment on Morbidity and Mortality in Central Nervous System Tuberculosis (CNS-TB)

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Background and aims: CNS-TB is treated with an antituberculosis drug regimen compromised of intensive and continuation phases. CSF: Serum sugar ratio is used as a surrogate to assess the clinical response to treatment. Persistent low CSF: Serum sugar is used as an indication for extending the intensive phase. This study aimed to assess the response of the intensive phase of antituberculosis treatment concerning CSF sugar drop in patients with TB Meningitis.

Methodology: An observational prospective study with the participation of 44 adult patients with TB Meningitis with a sugar drop of at least 50% before starting treatment. CSF was assessed at the diagnosis, 2 months and 1 year. Intensive phase treatment was continued for an extra month in those having CSF: Serum sugar 0.5 at 2 months.

Results: The mean age was 35.18 ± 16.7 years. The majority (72.7%,n=32) had GCS grade 2 on admission. 95.5% (n=42) had 0.5 CSF: Serum glucose ratio at the time of diagnosis. At 2 months, 61.4% (n=27) had CSF: Serum glucose

Conclusion: CSF: Serum sugar ratio can be used to monitor response to treatment. Extended intensive

phase in persistent low CSF: Serum sugar ratio patients has shown a favourable outcome.

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Unilateral hypoglossal nerve palsy as an isolated symptom of internal carotid artery dissection: A case report

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Background: Internal carotid artery dissection (ICAD), caused by a spontaneous or trauma-related tear in the intimal layer of the carotid artery, is the most common cause of ischemic stroke in young and middle-aged adults. Only a few examples of ICAD causing isolated cranial nerve palsy with the hypoglossal nerve affected were presented in the literature.

Case Description: A 39-year-old male presented with tongue swelling, difficulty speaking, difficulty chewing and swallowing bolus, and voice disorder. He had a history of whiplash injury a few years ago, as well as neck trauma 10 months ago and a strong occipital headache five days before symptom onset. Physical examination showed dysphonia and macroglossia on the right side, without deviation in tongue protrusion or other neurological impairment. He received pyridostigmine as a diagnostic and therapeutic measure due to non-specific symptomatology, leading to subjective improvement. Routine laboratory investigations and tongue biopsy were normal. Meanwhile, CTA revealed no sign of ICAD, but pre- and post-contrast 3D TOF MRA showed a dissecting pseudoaneurysm of the right internal carotid artery with a diameter of approx. 14-15 mm located in front of the opening of the right canal of the hypoglossal nerve, which was the cause of the nerve lesion. The patient did not return for further examination after diagnosis. Two months after the MRA findings, he had an ischemic stroke caused by total occlusion of the right internal carotid artery.

Conclusion: Despite the rare presentation, the symptoms of the hypoglossal nerve lesion should be considered as a differential diagnosis of ICAD.

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Are Functional Neurological Disorders Feigned? Using Evolutionary Medicine to Explain the FNDs

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The FNDs are commonly encountered in neurological practice. They are believed to be unintentionally produced and genuinely experienced neurological symptoms. These symptoms and the disease course are incongruent with recognized organic neurological disorders. The examination findings (also termed positive criteria) distinguish them from organic disorders and are essentially the same findings as are seen in feigning (eg. Hoover sign and entrainment).

We present a description of the FNDs using evolutionary theory that calls into question the role of feigning. We hypothesize that they are not intentionally feigned but that this feigning is done unconsciously. This is accomplished by self deception.

With self deception the unconscious deceives the conscious self into believing functional symptoms are unintentional when they are in fact (unconsciously) intentional and meant to deceive an outside observer so as to hide unacceptable desires and intentions. The conscious self has little to no awareness of the self deception which is in keeping with the accepted unintentional nature of the FNDs.

Self deception is well described in evolutionary theory whereby the unconscious self effectively deceives the conscious self into believing something untrue about reality. Self deception is a simple and parsimonious explanation for the FNDs as they clearly appear feigned to the trained observer and the examination findings are indistinguishable from

feigning. Unconscious feigning retains the conscious unintentionality while adding the unconscious intentionality of the deception. We believe this hypothesis has great explanatory power for the etiology of FNDs and the potential to result in better treatments and outcomes.

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Evaluation of vestibulo-ocular reflex in spinocerebellar ataxias with slow saccades

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Introduction: The video head impulse test (vHIT) assesses the vestibulo-ocular reflex (VOR) by measuring the VOR gain and the compensatory catch-up saccades (CS). However, saccade generation is markedly impaired in certain subtypes of spinocerebellar ataxia (SCA). Thus, observing CS may not be informative in these cases. We investigated the clinical significance of CS in SCA patients with slow saccades using vHIT.

Methods: We consecutively enrolled 17 genetically confirmed SCA patients (men=9, mean age=29; SCA2=8, SCA7=9). The head impulse testing was performed in all subjects using a vHIT device. The VOR gain and the presence of CS were analyzed. The dysfunctions of saccades and other ocular motor findings were investigated using video-oculography.

Results: Horizontal and vertical saccadic slowing were common in SCA2 and SCA7 (15/17, 88.2%; SCA2=7, SCA7=8). Among 15 patients with saccadic slowing, 7 patients (46.7%; SCA2=1, SCA7=6) exhibited abnormally decreased VOR gains in at least one canal plane. Impaired VOR gain was common in the vertical canal planes (7/7, 100%), while it was infrequent in the horizontal canal plane (2/7, 28.6%). However, only one SCA7 patient showed compensatory CS in the horizontal plane. Despite frequent VOR gain impairments in the vertical canals, CS in these canal planes were absent.

Conclusions: According to our results, in SCA patients with saccadic slowing (mostly SCA7), impairments in VOR gain may not consistently result in compensatory CS, especially in the vertical plane. Therefore, a quantitative analysis of VOR gain using vHIT is necessary instead of relying on observing CS in these patients.

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Bilateral staged VIM thalamotomy for essential tremor

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Background: Unilateral MRI-guided focused ultrasound (FUS) has established efficacy in tremor relief. Data regarding the safety and efficacy of staged bilateral treatments is scarce.

Objective: To report preliminary results of a clinical trial to evaluate the safety and efficacy of unilateral FUS thalamotomy in essential tremor (ET) patients that previously underwent unilateral FUS treatment on the opposite side

Methods: Six patients that underwent unilateral FUS thalamotomy for medication refractory tremor at least 6 months before and had bothersome tremor on the un-treated side, underwent FUS treatment to relive tremor. Primary outcome was change in tremor score in the treated hemibody relative to baseline, using the Clinical Rating Scale for Tremor. Secondary outcome was change in quality of life in ET (QUEST) score relative to baseline. Adverse event profile was collected.

Results: Tremor score in the treated hemibody significantly improved following FUS from a median score of 16 (range 6-19) at baseline to median score of 0 at 1 month (range 0-6, p=0.001). Quest score improved from a median baseline score of 23 to a score of 8.5 at 1 month. At 1 month adverse events included: mild ataxia (n=6), dysgeusia (n=1), lip and tongue paresthesia (n=1).

Conclusions: Our preliminary results suggest that staged bilateral magnetic resonance-guided focused ultrasound thalamotomy was effective and safe and

improves the tremor and quality of life of patients with ET. Larger studies and longer-term follow-up are needed to validate these findings.

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Unilateral Facial Nerve Palsy: When to do a Lumbar Puncture?

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Background: Facial nerve palsy is the most common cranial neuropathy. In most cases it is idiopathic, being called Bell's palsy. It is also a typical presentation of Lyme neuroborreliosis as well as of other infectious and non-infectious inflammatory disorders.

Case presentation: We present the case of a 45-year-old male, without significant medical history, who presented for a left facial nerve palsy with sudden onset five days prior, at the end of July. He also had short episodes of ipsilateral mandibular numbness and contralateral tongue paresthesia. Over the past six weeks he experienced moderate holocranial headache with painful C2 paroxysms, improved by NSAIDs. He denied tick bites, skin lesions suggestive of erythema migrans or recent febrile illness but spent several hours per week in nature. At admission, the neurologic examination was normal except for the left peripheral facial nerve palsy. Considering the accompanying red flags, we performed a diagnostic lumbar puncture and a brain MRI. The cerebrospinal fluid (CSF) examination revealed high lymphocytic pleocytosis with hyperproteinorahia, while the brain MRI showed mild symmetrical contrast enhancement of multiple cranial nerves. The extensive etiopathogenic workup found positive Ig M and Ig G Borrelia antibodies in serum and CSF, with intrathecal synthesis, prompting a diagnosis of Lyme neuroborreliosis. The patient fully recovered with antibiotic treatment.

Conclusion: In patients with facial nerve palsy the presence of red flags should prompt a lumbar puncture. Lyme neuroborreliosis should be suspected and evaluated in patients with facial nerve palsy if there is any possibility of tick exposure.

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Personality profile of patients with major depressive disorder and fibromyalgia

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Introduction: Fibromyalgia (FM) is a common comorbidity of major depressive disorder (MDD) that negatively affects social and clinical outcomes. However, it remains understudied whether the personality profile of patients with MDD and FM differs from those with MDD only in terms of the maladaptive personality traits listed in ICD-11 and DSM-5TR.

Methods: We conducted a case-control study: 66 patients with MDD+FM were compared with 66 age- and sex-matched MDD patients without FM. The mean age of the participants was 56.4 (14.9) years; 89.4% were female. MDD was diagnosed by a psychiatrist using the Mini-International Neuropsychiatric Interview, and FM was diagnosed by a neurologist using the 2016 American College of Rheumatology diagnostic criteria. All patients completed the Modified 36-Item Personality Inventory for DSM-5 and ICD-11 Brief Form Plus-Modified (PID5BF+M), the Beck Depression Inventory

(BDI), and the State-Trait Anxiety Inventory (STAI). Mann-Whitney U-test, Chi-square test, Benjamini-Hochberg correction, Common Language Effect Size Evaluation (CLES) were statistical methods.

Results: No differences were found between the groups in education level, marital and employment status, BDI and STAI scores (p0.05). MDD+FM patients had significantly higher scores in the following domains: Negative Affectivity (3.72(1.08) vs. 2.81(1.41): p0.001, CLES0=0.69), Detachment (2.77(1.34) vs. 1.67(1.24): p0.001, CLES=0.73), Antagonism (1.84(1.11) vs. 1.30(1.27): p=0.001, CLES=0.66), Disinhibition (2.40(1.15) vs. 1.73(1.17): p0.001, CLES=0.67), Anankastia (2.88(1.64) vs. 1.73(1.39): p0.001, CLES=0.70), Psychoticism (1.98(1.45) vs. 0.72(1.06): p0.001, CLES=0.77).

Conclusion: FM in MDD patients is associated with higher scores in all trait domains listed in ICD-11 and DSM-5TR, with the largest effect sizes found for Psychoticism and Detachment.

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Shedding Light on the Atypical: Burning Mouth Syndrome (BMS) as an Initial Presentation of Idiopathic Basal Ganglia Calcification (IBGC) - A Case Report

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Objective: To present BMS as a potential early symptom of IBGC.

Background: IBGC is characterized by calcium deposition in the basal ganglia, cerebral, and cerebellar cortical regions. It may be either familial or sporadic, with various clinical signs, including progressive dementia, pyramidal, extra-pyramidal, and cerebellar involvement. Limited information is available on non-neurological aspects of IBGC. Characteristic oral features, including missing teeth, tooth mobility, gingival inflammation, and gum recession with periodontitis, are rare. The literature contains only a sparse number of cases of BMS with IBGC.

Methodology/Design: Case Report.

Results/Case Presentation: A 75-year-old man with hypothyroidism and RLS came to the clinic after six months of chronic tongue burning, preceded by penile pain. Further questioning revealed progressive non well non-described cognitive decline. Brain CT and MRI, without contrast, showed periventricular, basal ganglia, and cerebellar mineralization. Serum levels of PTH, TH, and ionized calcium were normal. Trigeminal SEP revealed bilateral conduction slowing. The patient was prescribed Gabapentin, as clonazepam had adverse effects.

Conclusion: BMS is infrequently documented as an initial presentation of IBGC. While the causative role of calcium deposits in pain fibers remains debated, the involvement of basal ganglia/thalamic nuclei with subsequent failure of the striatal dopamine systems remains ambiguous. This case report contributes valuable insights into the association between BMS and IBGC and encourages further research to elucidate the intricate relationships between these distinctive pain syndromes and basal ganglia calcification. Further analysis in the context of prior reports will be the subject of a more detailed study.

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Serum Neurofilament Light Chain in COVID-19 and the Influence of Renal Function

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COVID-19 is associated with various neurological symptoms. Serum neurofilament light chain (sNfL) is a robust marker for neuroaxonal injury. Recent

studies have shown that elevated levels of sNfL are associated with unfavourable outcome in COVID-19 patients. However, neuroaxonal injury is rare in COVID-19, and renal dysfunction as well as hypoxia, both of which are known in severe COVID-19, can also increase sNfL levels. Thus, the meaning and mechanisms of sNfL elevation in COVID-19 patients remain unclear.

We evaluated sNfL levels in 48 patients with COVID-19 (mean age = 63 years) and correlated them to clinical outcome, the form of oxygen therapy, and creatinine. Levels of sNfL were age-adjusted and compared with normal values and z-scores. COVID-19 patients treated with nasal cannula had normal sNfL levels (mean sNfL = 19.6 pg/ml) as well as patients with high flow treatment (mean sNfL = 40.8 pg/ml). Serum-NfL levels were statistically significantly higher in COVID-19 patients treated with mechanical ventilation on intensive care unit (ICU) (mean sNfL = 195.7 pg/ml, p0.01). There was a strong correlation between sNfL elevation and unfavourable outcome in COVID-19 patients (p0.01). However, serum creatinine levels correlated directly and similarly with sNfL elevation and with unfavourable outcome in COVID-19 patients (p0.01). Additionally, multivariate analysis for serum creatinine and sNfL showed that both variables are jointly associated with clinical outcomes.

Our results identify renal dysfunction as an important possible confounder for sNfL elevation in COVID-19. Thus, serum creatinine and renal dysfunction should be strongly considered in studies evaluating sNfL as a biomarker in COVID-19.

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Non-paraneoplastic Lambert-Eaton Myasthenic Syndrome – Case Report

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Introduction: Lambert-Eaton myasthenic syndrome (LEMS) is a rare condition affecting neuromuscular junction transmission, characterized primarily by muscle weakness as its main clinical presentation. LEMS is a condition characterized by diminished acetylcholine (ACh) release from the presynaptic nerve terminals, even though the ACh vesicle number, ACh presynaptic concentration, and postsynaptic ACh receptors are all within normal parameters.

Case Presentation: A 69-year-old male presented to the hospital with an acute onset of weakness, mainly affecting the facial and oro-pharyngeal muscles. On physical examination, dysarthria, dysphonia, and right-sided facial weakness were noted. The clinical course progressed acutely over a period of several days, culminating in shallow breathing with tachypnea and subsequently hypoxia, necessitating mechanical ventilation of the lungs. Upon laboratory and instrumental examination, a diagnosis of Lambert-Eaton myasthenic syndrome was made.

Results: The patient received plasma exchange in the inpatient setting, and after discharge, he was started on the combination of steroid and neostigmine therapy, with progressive improvement.

Conclusion: Even though LEMS most commonly presents with slowly progressive proximal muscle weakness, particularly involving the legs, one should not rule out this disease even in cases where ocular symptoms, especially ptosis and diplopia, or bulbar muscle weakness predominate. Although rare, the latter symptoms may be presenting. Also, one should take into consideration that even though most patients do not have significant respiratory muscle weakness, a small minority like our patient may become dyspneic acutely

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Motor development in patients with cyanotic heart defects

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Introduction: The impact of congenital heart defects on the neurodevelopment of infants is being actively investigated with the aim of developing methods of early intervention. The purpose of the study is to evaluate the stages of stato-motor development of patients with cyanotic heart defects after surgical treatment.

Materials and methods: 39 patients with cyanotic congenital heart defects who underwent examination and surgical treatment with transposition of the main vessels and tetrad of Fallot were studied. The stages of stato-motor development were assessed us-

ing the following developmental scales: Hammersmith Infant Neurological Examination and Munich Functional Developmental Diagnosis, namely Sitting and Walking. The control group consisted of 20 healthy patients.

The results: For patients with cyanotic heart defects, a birth weight of 3315 (+/-535) and an average Apgar score of 7 points were characteristic. Surgical treatment for transposition of main vessels is performed on average on the first day, and for tetralogy of Fallot - at 8 months of life. The average duration of artificial blood circulation was 137 minutes (+/-28.92), the duration of aortic clamping was 69 minutes (+/-15.47). When assessing motor development, a delay in the stages of sitting and walking was found in 28% of patients.

Conclusions: Patients are born with a satisfactory body weight and a slightly reduced Apgar score. The delay in the onset of sitting and walking in 28% of patients can be attributed to the effect of moderate hypoxia on the development of the nervous system in children with tetrad of Fallot and recovery after surgical treatment, which is seen at the age of 8 months. It is timely early surgical treatment of critical transposition of main vessels in the first day of life after birth, techniques of performing operations - ensure their better stato-motor development in the future.

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Ultrasound Reference Values of Peripheral Nerve Cross-Sectional Area in the Lithuanian Population

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Objective: to present ultrasound reference values of peripheral nerve cross-sectional area (CSA) in healthy Lithuanian adults.

Methods: 125 participants (63 men, 62 women) underwent high-resolution ultrasound of peripheral nerves. Nerve CSA was measured at sites predefined by polyneuropathy protocols. Results were checked for association with age, sex, weight, and height.

Results: the following nerve CSA values (mean±2SD) were obtained: 5th cervical root (5.9±2.9 mm2), 6th cervical root (8.3±3.5 mm2), vagus nerve (1.7±0.8 mm2), median nerve in the carpal tunnel (7.8±3.4 mm2), median nerve in the forearm (5.0±1.6 mm2), median nerve at the elbow (5.5±2.0 mm2), median nerve in the upper arm (8.0±2.9 mm2), ulnar nerve in the Guyon canal (4.5±1.7 mm2), ulnar nerve in the forearm (4.1±1.7 mm2), ulnar nerve at the elbow (6.0±3.0 mm2), ulnar nerve in the upper arm (5.1±2.0 mm2), radial nerve in the spiral groove (3.8±1.3 mm2), superficial radial nerve (1.2±0.5 mm2), tibial nerve in the popliteal fossa (24.3±10.9 mm2), tibial nerve at the malleolus (8.5±4.1 mm2), peroneal nerve in the popliteal fossa (4.8±1.9 mm2), superficial peroneal nerve (1.7±0.8 mm2), sural nerve at the malleolus (1.6±0.8 mm2), sural nerve in the calf (1.6±0.7 mm2). Men had larger nerve CSA compared to women in the majority of measured sites. Some associations between age, weight, height, and CSA were also found.

Conclusion: Ultrasound is a useful tool in the diagnosis of inflammatory polyneuropathies. To differentiate pathology from normal variations it is necessary to have normative values. We present ultrasound reference values of peripheral nerve CSA in healthy Lithuanian adults.

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