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Alzheimer's Disease & Dementia

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From Perception to Plate: Exploring Mediterranean Diet and Dementia Prevention Through the Health Belief Model

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Background: Dementia is incurable; however, it can be prevented by adopting certain health behaviors, particularly following the Mediterranean diet (MD). This study had two main objectives: (i) to assess the adherence to the MD in individuals aged 50 and above who were born in Israel, and (ii) to investigate the relationship between variables of the Health Belief Model (Rosenstock, 1966, 1974) and adherence to MD.

Method: This cross-sectional study utilized an online convenience sampling in 2022-2023. The study included 512 Israel-born participants aged 50 years or older. MD was assessed using I-MEDAS (Israeli Mediterranean Diet Adherence Screener (Abu-Saad et al., 2018). Cognitive perceptions were assessed using the Motivation to Change Lifestyle and Health Behaviors for Dementia Risk Reduction questionnaire (Kim et al., 2014).

Results: In the current research, the average score concerning the MD was 9.35 (1.36 SD) out of 17 possible points. A multivariate linear regression indicated that among all of the Health Belief model's variables, perceived severity (β=-.204, p.001) and cues to action (β=.194, p.001) emerged as significant predictors of adherence to MD. Additionally, being female (β=.192, p.001) and having a low income (β=-.156, p.05) were also found to predict adherence to the MD. The model explained 15.7% of the variance in the adherence to MD [F(4,505)=15.56, p.001].

Conclusions: The current research underlines the role of health cognitions (perceived severity and cues for action) regarding adherence to MD. The results of the current study might serve as a basis for intervention programs among various target populations.

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Rapid amyloid clearance and efficacy: Results from TRAILBLAZER-ALZ 2, a phase 3 study of donanemab for treatment of early Alzheimer`s disease

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Background: The aim of this analysis was to explore the impact of rapid amyloid clearance (rAC) on downstream biomarkers and clinical efficacy.

Methods: In TRAILBLAZER-ALZ 2, participants were randomized to receive (1:1) donanemab (n=860) or placebo (n=876) intravenously every 4 weeks (w) for 72w. Donanemab-treated participants were determined as achieving rAC during the trial if the brain amyloid level was below 24.1 Centiloids at either 24w or 52w as measured by amyloid PET (positron emission tomography). Propensity score matching method was used to select matched placebo-treated participants comparable with donanemab-treated participants with rAC in terms of baseline age, amyloid level, global tau level, and number of APOLIPOPROTEIN ε4 alleles (mPlacebo). At 76w, the biomarker and clinical measurements were compared between the two matched groups.

Results: The rAC group had significantly less accumulation of tau (AD-signature-weighted neocortical SUVr as determined by PET) at 76w compared to mPlacebo [adjusted mean (SE) change from baseline: 0.0684 (0.006) for mPlacebo, and 0.0461 (0.006) for rAC, difference (SE): -0.0223 (0.008), P=0.007]. The adjusted mean change from baseline of plasma P-tau217 and plasma glial fibrillary acidic protein were both significantly different from mPlacebo (0.001). Adjusted mean change in integrated AD Rating Scale score (SE) at 76w was -11.5 (0.62) in the mPlacebo group, and -7.6 (0.62) in the rAC group [adjusted mean difference from mPlacebo, 3.86 (0.89) P0.001], representing a 33.6% slowing of disease progression.

Conclusion: These results demonstrate the downstream effect of donanemab-induced rAC on biomarker and clinical efficacy measurements.

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Beyond Traditional Screening: AI-Driven Early Detection of Cognitive Disorders and Dementia

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In Hungary, the process of diagnosing dementia is slow and time-consuming. Currently, there are no well-developed systems and strategies at the local level for screening, and there is no artificial intelligence algorithm that could determine early signs of dementia based on the patient`s digital behavioral patterns.

Two PILOTs were conducted using the PreDem platform. Over the PILOTs` duration (2021.09.01.-2024.01.11), 42,711 test data were analyzed. The 259 participants completed SDMT-type tests, Stroop tests, and memory/word games.

We established a unified system for task evaluation, facilitating cross-test result comparisons. Participants were grouped into three categories: 1st - presumed dementia patients, 2nd - diagnosed MS patients, and 3rd - presumably normal population. Comparing the first two groups to the normal population revealed significant differences, vividly illustrated by density functions. Our results show that the first symptoms of dementia can appear as early as the 20s-30s, and can be clearly detected in the 40s and 50s.

The platform used in the study is a promising new tool for the early detection and prevention of dementia. During the PILOT studies, the platform reliably identified dementia patients, significantly surpassing the accuracy of traditional diagnostic methods. Therefore, it can be said that this method is suitable for detecting the first, otherwise unnoticed signs of dementia through risk analysis based on artificial intelligence processing. Early detection is crucial for effective management of dementia. Early diagnosis allows patients to begin necessary treatments, which can slow the progression of the disease, preserve cognitive functions, and improve quality of life.

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Association Between Body Mass Index and the Survival in Older Patients with Dementia

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Objectives: The aim of our study was to identify the peculiarities of survival depending on body mass index (BMI) in patients with dementia and eating disorders. Methods. Cross-sectional observational study was performed from 2020 to 2023 in palliative clinic “Palmedi” of Tbilisi State Medical University. The study group consisted of 77 patients with dementia (18 males, 59 females; mean age - 78.0 □ 11.1). Dementia was assessed by Mini-Mental State Examination (MMSE) and Clinical Dementia Rating (CDR) scale. Serum resistin levels were measured by enzyme-linked immunoessay (ELISA). The study group was divided by the three groups according BMI values: the group 1 (BMI25 kg/m2; n=12; 15.6%). Survival rates during 25 weeks of the study were assessed by the tools of survival analysis.

Results:. 25-weeks survival rate for the study group was 20.8%. 50%-survival was observed on 7th week of the study. The survival rate for the group 1 was 13.6%; for the study group 2 – 28.6%, and for the study group 3 – 33.3%. 50%-survival 50%-survival for the study group 1 was observed on 6th week of the study, for the study group 2 - on 14th week of the study; for the study group 3 - on 20th week of the study. Hazard ratio (HR) between the groups 1 and 2 was HR=1.78 (95%CI – 1.03-3.09, p=0.047); between the groups 1 and 3 was HR=2.38 (95%CI – 1.29-4.41, p=0.021); between the groups 2 and 3 was HR=1.40 (95%CI – 0.62-3.21, p=0.435)

Conclusion: BMI had impact on the survival rates of the patients with dementia. Therefore, decreased values of BMI may be considered as a predictor of bad outcome.

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The effect of different donanemab dosing regimens on ARIA-E and amyloid lowering in adults with early symptomatic alzheimer's disease: primary outcome results from TRAILBLAZER-ALZ 6

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Background: Amyloid-related imaging abnormalities (ARIA) have been observed with amyloid-targeting therapies, including donanemab. TRAILBLAZER-ALZ 6 (NCT05738486) assessed the impact of different donanemab dosing regimens on the frequency of ARIA-E in relation to amyloid reduction.

Methods: This was a multicenter, randomized, double-blind, phase 3b study in adults with early symptomatic AD. Participants (n=843) were stratified by APOE genotype and baseline amyloid levels and randomly assigned to the standard dosing arm or one of 3 alternative dosing arms in a 1:1:1:1 ratio. Relative risk reduction of ARIA-E by week 24 was analyzed through Bayesian logistic regression. Brain amyloid level (as measured by positron emission tomography) and plasma P-tau217 level were also assessed.

Results: By week 24, the frequency of ARIA-E was 23.7% for the standard dosing arm, and 18.6%, 13.7%, and 18.3% for the 3 alternative dosing arms. The modified titration dosing regimen with the lowest ARIA-E (13.7%) had a 41% reduction in the relative risk of ARIA-E compared to the standard dosing arm. The ARIA-E radiographic severity in the modified titration arm was significantly less. The symptomatic ARIA-E frequency was 2.8% in the modified titration arm compared to 4.8% in the standard arm. Participants had significant amyloid reduction with adjusted mean (SE) change of 58.8 (1.8) Centiloids in the standard arm, 56.3 (1.7) in the modified titration arm. Plasma P-tau217 reductions at 24 weeks were similar in all dosing arms as well.

Conclusions: This study suggests that a modified titration approach may limit ARIA risk while maintaining sufficient amyloid reduction.

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Efficacy of Ipidacrine in Enhancing Cognitive Function and Quality of Life in Mild Cognitive Impairment: A Single-Blind Randomized Controlled Trial

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Background: Ipidacrine, a reversible acetylcholinesterase inhibitor, enhances cholinergic neurotransmission by inhibiting acetylcholinesterase and blocking potassium channels, facilitating impulse transmission in the central nervous system. Preclinical studies have demonstrated ipidacrine`s potential in improving memory and cognitive functions. This study evaluates the efficacy of ipidacrine in enhancing cognitive function and quality of life (QoL) in patients with mild cognitive impairment (MCI).

Methods: This single-blind, randomized controlled trial aims to enroll 102 ambulatory patients aged ≥50 years diagnosed with MCI (MMSE score ≥19). Participants are randomized into two groups: an intervention group receiving ipidacrine and a control group receiving standard care. Randomization is conducted via an electronic platform to ensure unbiased allocation. Cognitive function is assessed using the Mini-Mental State Examination (MMSE), and QoL is evaluated with the DEMQOL questionnaire at baseline, 3 months, and 6 months. Independent evaluators, blinded to group assignments, conduct all assessments to minimize bias.

Results: As of now, 45 participants have been enrolled. Preliminary analyses suggest that the ipidacrine group demonstrates improvement in MMSE scores and DEMQOL ratings compared to the control group. The treatment has been well-tolerated, with no significant adverse effects reported. Ongoing statistical analyses are accounting for potential confounders such as age and education level.

Conclusions: Early findings indicate that ipidacrine may improve cognitive function and QoL in patients with MCI. The completion of this single-blind trial with the full cohort will provide robust evidence regarding ipidacrine`s therapeutic potential in MCI management.

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Identification and evaluation of potential microRNA markers for diagnostics in Neurodegenerative Diseases and correlation with other biochemical markers

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Objectives: MicroRNAs are short, non-coding RNA molecules essential for organism development and various biological processes. They are potential biomarkers for numerous diseases. This study aimed to identify microRNA targets that can differentiate neurodegenerative diseases and establish correlations between selected miRNAs across diagnostic groups.

Methods: The study included the analysis of 126 patients. The patients were divided into five diagnostic groups: Alzheimer's disease, non-Alzheimer's dementia, Movement disorder, Dementia and movement disorder, and Healthy controls. The circulating RNA was isolated using the iCatcher Circulating cfRNA 1000 Kit with the iCatcher 12 automated isolator. The determination of microRNA was performed by TT-qPCR in the CFX96™ Real-Time Detection System. The concentrations of the remaining biomarkers were determined by ELISA. The statistical data were processed using MS Excel and MedCalc® software.

Results: The following microRNAs were studied based on the primary screen for identification of potential microRNA targets and published literature data:hsa-miR-23a-3p, hsa-miR-29c-3p, hsa-miR-30b-5p, hsa-miR-142a-5p, hsa-miR-146a-5p, hsa-miR-151a-3p. A statistically significant correlation was identified between hsa-miR-29c-3p and hsa-miR-30b-5p, hsa-miR-30b-5p and hsa-miR-151a-3p, hsa-miR-23a-3p and hsa-miR-29c-3p, hsa-miR-23a-3p and hsa-miR-151a-3p, between hsa-miR23a-3p and hsa-miR-30b-5p, between hsa-miR-142a-5p and hsa-miR-146a-5p, hsa-miR-142a-5p and hsa-miR-151a-3p, between hsa-miR-146a-5p and hsa-miR-151a-3p. Significant differences were observed in hsa-miR-23a-3p and hsa-miR-29c-3p among different diagnostic groups. Compared to classical biomarkers of dementia, significant correlations were observed between plasmatic amyloid-β peptide 42 and hsa-miR-29c-3p, hsa-miR-142a-5p, hsa-miR-146a-5p, hsa-miR-151a-3p.

Conclusions: The most promising microRNAs for differentiating among neurodegenerative diseases are hsa-miR-23a-3p and hsa-miR-29c-3p. Additionally, there is a correlation between hsa-miR-29c-3p and amyloid-β peptide and the ratio of amyloid-β peptide 42/40.

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Feasibility and Efficacy of GOLD-Cog+: a novel combined cognitive intervention for healthy older adults

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Background: With dementia cases projected to reach 78 million by 2030 and 139 million by 2050, effective prevention strategies are urgently needed. Cognitive training based on neuroplasticity principles can enhance cognitive reserve, potentially delaying cognitive decline and preserving functional independence. While computerized cognitive training (CCT) improves cognition in healthy older adults, its impact on daily functioning remains mixed. This study examined the feasibility and efficacy of GOLD-Cog+, a novel approach combining individual CCT with group goal-directed training, in improving cognitive, affective, and functional abilities.

Methods: Sixty-five community-dwelling older adults (age ≥65) with at least sub-clinical depression (PHQ-8 ≥ 5) and minimal or no cognitive decline (MoCA ≥ 20) were recruited to a randomized controlled crossover trial. Participants completed baseline assessments, were randomized to GOLD-Cog+ or a waitlist for six weeks, and then crossed over to the opposite group, concluding with follow-up assessments. Outcome measures included cognitive control, daily functioning, depressive symptoms, subjective cognition, rumination, anxiety, and quality of life.

Results: Of the 151 participants approached, 65 completed baseline assessments (43% recruitment), 59 were randomized, and 56 completed post-intervention assessments (95% retention). Participants reported high satisfaction with the intervention. A small but significant improvement in cognitive control was observed ($t(51) = 3.58$, p 0.001; mean difference = 0.18).

Conclusion: GOLD-Cog+ demonstrates excellent feasibility, high retention, and initial efficacy in older adults. This cost-effective intervention has the potential to preserve cognition, improve mental health, and enhance daily functioning in older populations.

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Will Lecanemab Improve Outcomes for Patients with Alzheimer's Disease?

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder and the most common cause of dementia. While current treatments, such as cholinesterase inhibitors like Rivastigmine, offer symptomatic relief, they do not significantly alter disease progression. In recent years, disease-modifying therapies (DMTs), particularly monoclonal antibodies (MABs), have shown potential in slowing the progression of the disease by targeting amyloid-beta (Aβ) plaques, a hallmark of AD pathology.

This poster evaluates the efficacy of Lecanemab (MAB), in slowing cognitive decline compared to standard-of-care (SoC) treatments and placebo. Research papers were collated using journal databases, with the search term 'Lecanemab', filters were applied to the search to find relevant articles about Lecanemab and its effect on clinical outcomes. Phase 2 double-blind clinical trials assessed Lecanemab's impact using the Alzheimer's Disease Composite Score (ADCOMS) and volumetric MRI analysis. Results showed a 28.5% reduction in clinical decline at an 18-month endpoint in patients receiving Lecanemab. MRI findings suggest reduced hippocampal atrophy and brain volume loss in the Lecanemab group.

Long-term outcome predictions, using simulation models, suggest that Lecanemab combined with SoC could extend survival by 1.03 years and improve quality-adjusted life years (QALYs) by 0.75 years. Patients on this regimen also demonstrated prolonged independence, spending an estimated 11.6 more years in community care.
Despite promising findings, limitations include reliance on modeling for long-term projections and the need for further investigation into hyperphosphorylated tau accumulation. Phase 3 trials are essential to validate these results, but this research highlights a potential breakthrough in AD treatment

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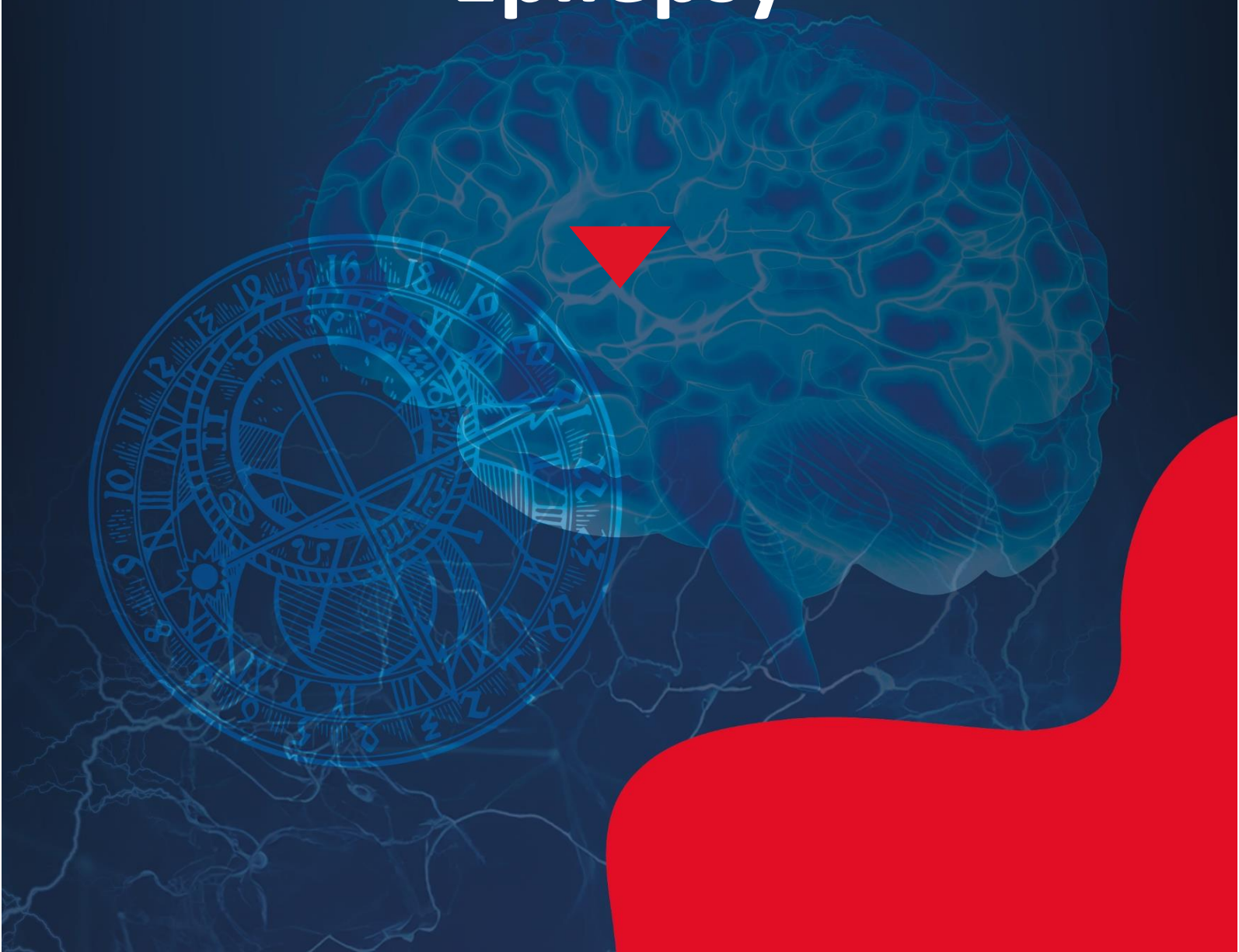
Epilepsy



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Changes in gut microbiome can be associated with abrupt seizure exacerbation in epilepsy patients

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Purpose: Seizures can be triggered by a variety of endogenous or exogenous factors. We hypothesized that alterations in the gut microbiome may be a seizure precipitant and analyzed the composition and characteristics of the gut microbiome in epilepsy patients who experienced an abrupt seizure exacerbation without a clear seizure precipitant.

Methods:

We prospectively enrolled 25 adult patients with epilepsy and collected fecal samples on the admission and after seizure recovery for next-generation sequencing analysis. We performed nonparametric paired t-test analysis to evaluate changes in the gut microbiota as seizures worsened and when it recovered and also estimated alpha and beta diversities in each category.

Results:

A total of 19 patients (13 males) aged between 19 and 78 years (mean 45.2 years) were included in the study. The composition of the gut microbiota underwent a significant change following an abrupt seizure exacerbation. At the phylum level, the relative abundance of Fusobacteria and Synergistetes was decreased in the seizure recovery state compared to the acute seizure exacerbation. A similar trend was observed at the lower hierarchical levels, with a decrease in the relative abundance of Fusobacteria, Tissierellia, and Synergistia at the class level, and that of Synergistales, Tissierellales, and Fusobacteriales at the order level. At the family level, the relative abundance of Fusobacteriaceae and Staphylococcaceae was decreased, whereas that of Leuconostocaceae was increased. No statistical differences were observed in alpha and beta diversity between the pre- and post-acute seizure exacerbation periods.

Conclusion:

Our study suggests that the changes in Fusobacteriaceae and Lecuonostocaceae may be associated with acute seizure exacerbation in epilepsy patients. Given that Fusobacteriaceae are associated with various systemic diseases due to their invasive properties and that Leuconostocaceae are known to produce GABA, our results may suggest a gut microbiome-based treatment option for epilepsy patients.

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Septic shock and convulsive status epilepticus in a patient with MELAS syndrome: A case report

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Background

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) is one of the most common maternally inherited mitochondrial disorders. While it is a heterogeneous syndrome with diverse clinical features, the most frequent presentation of central nervous system (CNS) involvement are epileptic seizures which can develop into status epilepticus (SE), often refractory.

Case presentation

A 29-year-old male patient, who had been diagnosed with MELAS two years prior, was transferred to our clinic due to convulsive status epilepticus. On admission, he was in a state of septic shock, with an altered mental state, verbally unresponsive, and was immediately admitted to the neurological intensive care unit. After a failure of seizure termination with intravenous antiepileptics, and due to respiratory insufficiency, he received analgosedation, after which he was intubated and mechanically ventilated. Brain MRI findings included irregular T2/FLAIR hyperintensities most prominent in the right parietal and temporooccipital region and the left occipital and temporal region, as part of the underlying condition. Initial EEG showed generalized slowing of background activity, with diffuse epileptiform abnormalities and an epileptic focus in the right fronto-centro-temporal regions. After the stabilization of his condition, correction of antiepileptic therapy (AET) was performed and physical therapy was initiated. He was discharged fully conscious, mobile with assistance, with right peripheral facial palsy.

Conclusion

Although we presented a patient whose condition improved significantly after status epilepticus, its onset in mitochondrial encephalopathies is usually associated with poor prognosis. Unraveling the mechanisms of epileptic seizures in MELAS is needed to develop more effective treatments

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The effect of ventral tegmental stimulation on the course of local seizure reactions induced by hippocampal stimulation.

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Mood disorders are the most frequent psychiatric comorbidity in epilepsy, and in particular in temporal lobe epilepsy. Emotional disturbances in patients with epilepsy can be: preictal - which develops before the onset of seizures, and interictal - which develops between seizure manifestations. It is especially noteworthy that pre- and interictal emotional disorders in patients with epilepsy can have both negative and positive manifestations. Clinical and especially experimental research shows that the factors that alter the emotional state of humans or animals affect the development/course of seizure activity. The results of such studies are contradictory. The limited number of studies does not allow us to conclusively establish whether there is a relationship between these emotional disorders and epileptogenesis. The dopaminergic system of the brain stem is involved in the implementation of positive emotional reactions. Therefore, the influence of stimulation of the ventral tegmental area in the development of convulsive reactions caused by irritation of the hippocampus was studied. It was shown that electrical stimulation of the ventral cover blocks local convulsive reactions in the hippocampus. At the same time, it was shown that the inhibition of convulsive reactions lasts for several tens of minutes.

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Effects of stimulation of emotiogenic central structures on the development of seizure activity of the brain

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Emotional disturbances such as anxiety, fear, depression and aggression are often experienced by patients with temporal lobe epilepsy. These psychiatric symptoms may occur during or just after (postictal) a seizure; however, in some patients, they occur interictally (i.e. between seizures) and may profoundly change the individual's personality. There is a lack of evidences regarding the influence of activation of emotiogenic structures and emotional behavior on development of seizures. The interrelation between emotional and seizure reactions was studied in Wistar albino rats. In our study we tried to elucidate: can emotional behavior evoked by stimulation of the emotiogenic zones of the hypothalamus or of induction of acute pain stress modify manifestations of generalized seizures within the period where a "full" epileptic syndrom has been stable formed earlier? Our leading hypothesis is as follow: the emotional disturbances can be considered as the emergence of instinctive behavior with an adaptive significance of defense and as a by-product of the inhibitory processes that build up to protect against the future occurrence of seizures.Our experiments for the first time gave direct proofs of the statements that activation of the DMH resulting in initiation of emotional behavior (anxiety and fear) interferes with the development of seizure activity initiated by the kindling procedure.

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The effect of dorsomedial hypothalamic stimulation on the course of status epilepticus induced by hippocampal stimulation

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A few clinical observations allow one to suppose that patients manifesting seizures that result from hyperactivation of the limbic structures are especially predisposed to interictal behavioral emotional disorders. The respective shifts in the emotional sphere can significantly modify the patient's personality. The mechanisms responsible for susceptibility to mental disorders in subjects suffering from epilepsy remain mostly obscure. In our study, we tried, to elucidate whether induction of emotional behavior resulting from stimulation of the dorsomedial hypothalamus (DMH) influences the development of seizure activity in the course of epileptogenesis within the framework of self-sustained status epilepticus (stimulation of the hippocampus). To induce hippocampal self-sustained status epilepticus, the animals (n=8) were subjected to the stimulation of ventral hippocampus with 10 sec train of stimuli, according to the following time schedule for total of 9 epochs (10 min each). The 10 min epoch consisting of 9 min stimulation and 1 min rest period, repeated 9 times within 90 min. In the trial group, the animals were subjected to the DMH along with hippocampal stimulation, only the DMH was stimulated (100-150 μA, 50-60 Hz) continuously (1 min) during the silence (hippocampal stimulation-off) period. Stimulation of the DMH in the above experimental situations resulted in significant suppression of both electrographic and behavioral manifestations of seizure activity.

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The effect of ventral tegmental stimulation on the course of generalized convulsive reactions induced by hippocampal stimulation.

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Emotional disturbances in patients with epilepsy can be: ictal - which accompany seizures, peri ictal - which develop after the seizures, preictal - which develop before the onset of seizures, and interictal - which develop between seizure manifestations. The relation between emotions and epileptic activity relies largely on exiguous clinical investigations. Consequently, the empiric and/or neurophysiological evidence for the possible relation between emotions and epileptic activity remains poorly known to date. Therefore, the effect of stimulation of the ventral tegmental area on the development/course of hippocampal stimulation evoked kindling was studied. It has been shown that stimulation of the ventral tegmental area inhibits the development of kindling induced by hippocampal stimulation. Stimulation of the ventral tegmental area also inhibits the development of epileptogenic foci by irritation of the hippocampus in the presence of an already formed epileptogenic focus. The results obtained may be caused by the potentiation of dopaminergic neurons in the ventral tegmental area. It is also possible that neurons of the reticular nucleus of the thalamus participate in the blockade of seizure responses. It has been shown that activation of neurons of the reticular nucleus of the thalamus leads to a blockade of the development of generalized seizure responses.

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Interaction between Seizure and Theta Rhythm

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Recently it was shown by us that combined stimulation of hippocampus and dorsomedial hypothalamus resulted in suppression of the electroencephalographic seizure reactions and, respectively, manifestations of behavioral seizures reduced. It is expected, that augmentation of inhibitory processes in hippocampal neurons in the course of dorsomedial hypothalamus stimulation can trigger mechanisms preventing the development of epileptiform activity. Because of two important characteristics of the hippocampus—theta rhythm and epileptogenesis—these appear to be interrelated in respect of their cellular substrates, and as far as theta rhythm may modulate hippocampal excitability, a study of the functional relationship between theta rhythm and seizure activity was endeavored. The purpose of this study is to test this proposal by determining the effects on seizures of induction or suppression of hippocampal theta activity. Our findings show that 1) the frequency of hippocampal interictal epileptiform dischargers increased with the transition from the awake state to drowsiness and a slow-wave sleep phase. After the animal came from slow-wave sleep to paradoxical sleep, epileptiform activity completely disappeared; 2)When at hypothalamus stimulation instead of theta rhythm the electrical activity is desynchronized, there occurs a considerable intensification of seizure activity. Therefore, seizure-theta antagonism in our experiments could be interpreted as an adjustment of the inhibitory mechanisms when the theta rhythm is evoked.

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Effect of Negative Emotional Reactions on the Development of Seizures in a Kindling Model in Rats

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We studied the effect of acute stress induced by nociceptive stimulation of the limbs on the duration of electroencephalographic epileptiform activity and manifestation of generalized motor convulsive reactions under conditions of a kindling model of epilepsy in rats. Two and four weeks after termination of the kindling procedure, test stimulations of the hippocampus evoked intense attacks of epileptic activity. Short-lasting pain-inducing stimulation (intense electrical stimulation of the limbs) resulted in noticeable limitation of both ECoG and motor behavioral manifestations of epileptic activity determined by the formation of an epileptogenic nidus. The antiepileptic effect of acute stress was limited in time; manifestations of this effect reached their maximum about 3 h after painful stimulation, while about 6 h after such stimulation they became smoothed to a considerable extent.

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Epilepsy in patients with depression after hemorrhagic stroke

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Objective: Depression and epilepsy are recognized complications following hemorrhagic stroke. This study aimed to evaluate the risk of epilepsy in patients with post-stroke depression.

Methods: This is a retrospective cohort study including hemorrhagic stroke patients diagnosed with depression in our center from April 2022 to November 2023. Patients with a prior diagnosis of depression or epilepsy were exluded. They were followed-up for a 12-month period with quarterly screening for clinical seizures. All patients had been started antidepressant treatment with either a SSRI or SNRI. Depression severity was evaluated using Hamilton Depression Rating scale (HAM-D). Statistical analysis included Chi-square test and logistic regression.

Results: A total of 103 patients was included who were diagnosed with depression after brain hemorrhage. Average mRS was 2.5 (SD 0.8) and HAM-D 13.1 (SD 4.5). Of these 63% were treated with a SSRI, 34.1% with a SNRI and 2.9% of patients had refused treatment or interrupted it due to early side effects. 19.4% of patients manifested seizures in the follow-up period, of which 45% focal seizures, 35% bilateral and 20% focal to bilateral. There was an increased frequency in the SSRI vs the SNRI group (22% vs 11%) which could suggest a trend towards a higher seizure risk with SSRI antidepressant however not statistically significant (p-value 0.057).

Conclusion: Post-stroke depression could be a risk factor for epilepsy. Study was limited by sample size, larger number studies needed to assess prevalence as well as differences among patients with different antidepressant medications or without therapy.

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Suicidality in persons with epilepsy: under the radar of depression screening

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Introduction:

It is often assumed that most people at risk of suicide have depression, and therefore the use of valid depression screening tools, such as the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E), is sufficient to effectively identify PWE at risk. The aim of our study is to assess whether scoring Item 4 of the NDDI-E separately from the total score of the NDDI-E adds value to screening for suicidality.

Methods:

A consecutive sample of Russian PWE admitted to the Center for Neuropsychiatry completed the NDDI-E and were assessed for suicide risk using the Columbia Suicide Severity Rating Scale (C-SSRS). Statistical methods used were Fisher`s exact test, Mann-Whitney test, Benjamini-Hochberg procedure.

Results:

A total of 372 PWE were enrolled (mean age 42.9 years, 64.8% female), of whom 42 (11.3%) were at risk for suicide according to the C-SSRS. In our sample, 31% of all suicidal patients had a total NDDI-E score below the cut-off for depression (12). With a cut-off of 1, Item 4 of the NDDI-E correctly identified suicide risk in 9 out of 13 PWE who scored positive for severe suicide risk on the C-SSRS but scored below the cut-off for depression on the NDDI-E.

Conclusion:

In routine practice, if decisions to refer a patient for psychiatric consultation were based solely on the total NDDI-E score, approximately 1/3 of at-risk PWE would not have access to appropriate psychiatric assessment and treatment. Our data support the utility of scoring Item 4 separately from the total NDDI-E score.

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Stress and seizures: The October 7th experience

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Background:

Stress is among the most frequently self-reported seizure-promoting stimulus of seizures in patients with epilepsy. Stress is a vague subjective concept that is hard to quantify or define empirically. Moreover, it often coexists with other seizure triggers, such as fever or sleep deprivation. To date, studies that investigated the prevalence of seizures during stressful events had conflicting results.

On October 7th, 2023, a large-scale terrorist invasion accompanied by massive rocket launching against Israel took place. These traumatic life-threatening events with widespread exposure, undoubtedly qualifies as a stressful crisis and provide an opportunity to investigate the possible role of stress in provoking seizures.

Methods: All adults who presented to the emergency department (ED) of Tel Aviv Sourasky Medical Center between January 1st 2017, and February 29th, 2024, and were diagnosed with seizures were included. Demographic and clinical parameters were collected using MDClone, a data acquisition tool. We compared the number of new and recurrent cases after the traumatic exposure between October 2023 and February 2024 to prior years.

Results: A diagnosis of seizure was given to 351 patients who presented to the ED after the traumatic. There was no difference regarding demographic variables compared to patients who presented in the same period the year before. A predictive model based on the number of ED presentations in previous years showed no difference in the period above compared to previous years. The results are unchanged when adjusted to the overall ED admissions from any cause.

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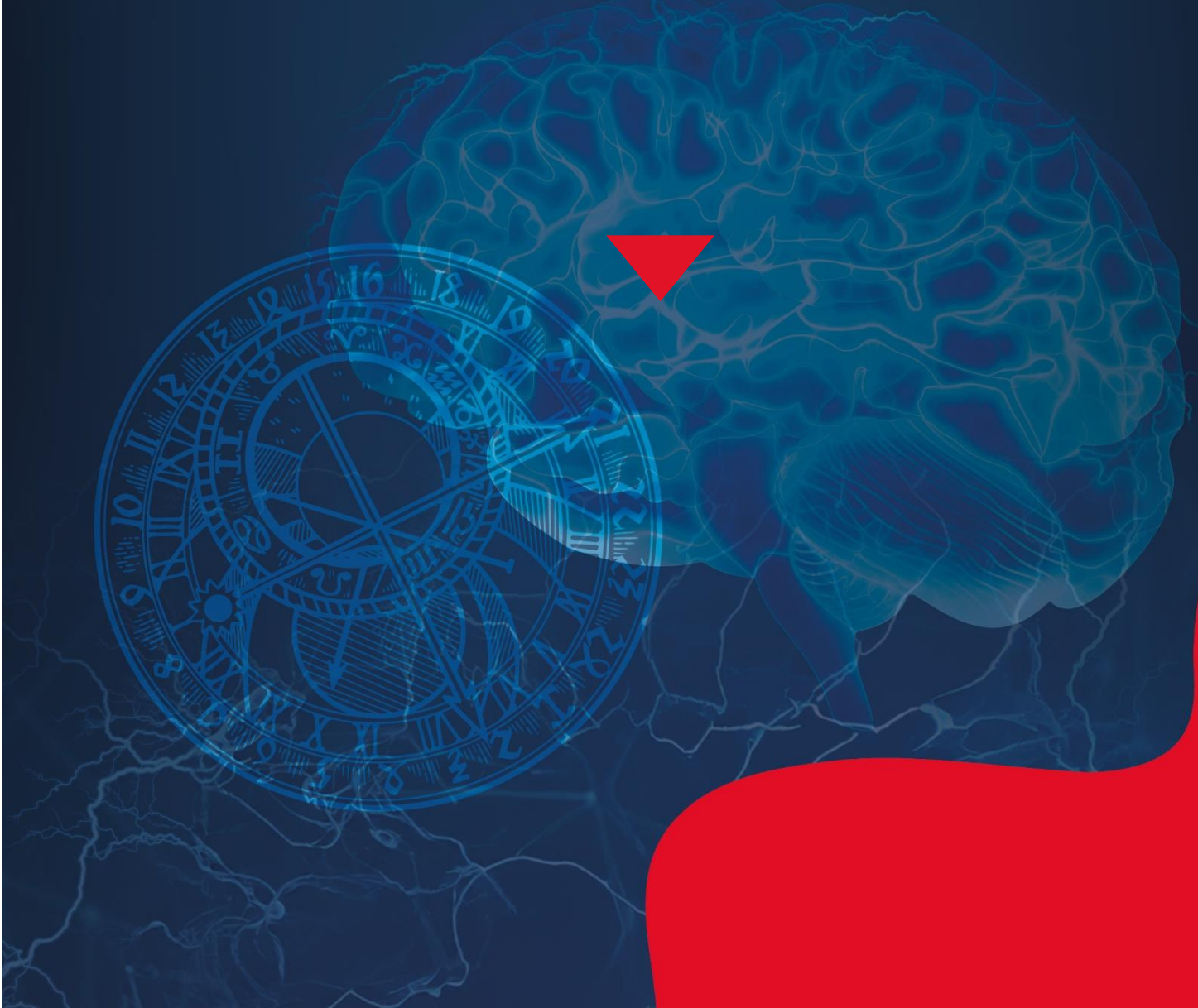
Headache



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Correlation of headache severity with screen time in patients with primary headache: a cross-sectional study

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Background:

Headache is the commonest neurological outpatient illness. With the advent of technology, increasing screentime has been shown to have effects on the occurrence of severity of headache. We aimed to determine the association of screentime with the type and severity of headache.

Methods:

In a single-center, cross-sectional study, patients with primary headache were enquired about the headache characteristics and screentime usage. The aim of the study was to determine the association of screen-time with headache severity in patients with primary headache. The co-factors studied were headache subtype, age, sex, frequency of headache.

Results:

In the study period (Sep2023-2024), there were 242 patients with primary headache. Majority were females (188(77.7%)) with median age 34.0(26.0;42.7) years. The commonest headaches were migraine (138(57.0%)), tension-type (69(28.5%)) and cluster (17(7.0%)). The commonest prophylactic medications were Tricyclic Antidepressants (95 (45.4%)) and beta-blockers (61(29.2%)). The commonest abortive medications were Naproxen (94 (46.0%)) and Paracetamol (71 (34.8%)).The Visual Analogue Scale VAS) of headache was 7.3 (6.0; 8.0). The screen-time was 192.7(35.0; 302.5) minutes. There was significant correlation of lower age with higher screen-time (Pearson's co-efficient p-value 0.001), and higher screen-time with worse VAS score (Pearson's co-efficient p-value 0.001). When the VAS score was adjusted for age, headache subtype and sex, the significant correlation was retained.

Conclusion:

There was a significant association of screentime with headache severity, when adjusted for age, sex, headache subtype and frequency. The deleterious impact of increased screentime needs to be further studied in longitudinal studies.

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Risk evaluation of OSA in Cluster Headache Patients using the STOP-bang questionnaire

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Objective:

To analyze the characteristics of cluster headache using the STOP-Bang screening for high risk of OSA and to define the characteristics of patients in relation to the risk of OSA using the STOP-Bang questionnaire in the cohort of cluster headache patients.

Methods:

This study was a retrospective analysis conducted at a single center, with patients enrolled between January 2019 and November 2022. Patients were diagnosed with cluster headache according to the criteria of the International Classification of Headache Disorders, 3rd edition (ICHD-3). The STOP-Bang screening was used to assess the presence of obstructive sleep apnea (OSA). These data were analyzed and compared based on the risk levels identified by the STOP-Bang screening.

Results:

Of 135 patients with cluster headache, 105 underwent STOP-Bang screening. The study cohort consisted mainly of 89 males (84.8%) with a mean age of 37.3 (±8.25) years. Of the 64 low-risk patients, 48 (75%) were male, while all intermediate- and high-risk patients were male. Body mass index was higher in the moderate- and high-risk groups than in the low-risk group, but there was no difference between the two groups (moderate- and high-risk). Current smokers were significantly more likely to be at high risk (64.9%) than former smokers (16.2%). There were no differences in other cluster characteristics, including average cluster and remission duration, diurnal and seasonal variation, and headache disability questionnaires based on the STOP-BANG score.

Conclusions:

Identifying obstructive sleep apnea (OSA) in cluster headache patients using STOP-Bang is useful to detect comorbidity of cluster headache characteristics.

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New headache after endacarotidectomy

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Headaches associated with CEA are not unusual. Etiology is not well defined, but is thought to be vascular, or due to damaged autoregulation of cerebral flow. Headaches often are in close relation with the time of surgery, mainly in the first week and mostly self-limited.

We performed a prospective study, to evaluate the characteristics of headache following CEA, conducted between January and July 2024, in 478 patients submitted to CEA. 70.7% of patients were male; mean age was 68.4 years-old. Headache incidence was 42.5%, ipsilateral to the CEA in 91% of patients; pressure type headache was the most common pain quality (85.2%) and affected the frontal region alone in 37.5% of headache episodes and diffuse in the others. Most were mild to moderate as intensity and without need of specific treatment, and relieved spontaneously 9.56 % (2 patients) severe throbbing headache, with migraine like qualities. One of them had hyper perfusion syndrome.

No correlation (p 0.05) was found between sexes and no significant value (p 0.05) was determined between the presence of headache and the mean degree of stenosis in the ipsilateral and contralateral carotid operated. History of previous TIA or stroke was the risk factor of post-CEA headache.

Conclusions: Headache following CEA is a common condition; in most cases it is ipsilateral to the procedure, pressure type, mild and self-limiting. When the headache is severe in patient with high state stenosis, should be evaluated the possibility of the hyperperfusion syndrome or cerebral infarction.

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Cortical Gray Matter Thickness Differences in Chronic Migraine Patients With and Without Medication Overuse Headache

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Objective: Prior studies using surface-based morphometric analyses have identified variations in cortical thickness among migraine patients. This study evaluates differences in cortical thickness in patients with chronic migraine (CM), comparing those with and without medication overuse headache (MOH).

Methods: Twenty-two CM patients with MOH and 13 without MOH underwent 3T MRI scans. T1-weighted structural images were acquired using an accelerated sagittal inversion recovery fast spoiled gradient echo sequence. Cortical thickness was analyzed using surface-based morphometry (FreeSurfer software). The study was approved by the Institutional Review Board, and all participants provided written informed consent.

Results: Significant differences in cortical thickness were observed between CM patients with MOH and those without. Patients with MOH exhibited alterations in multiple brain regions, including increased cortical thickness in nine regions and decreased thickness in six. Key regions affected included the anterior cingulate cortex (rostral and caudal), posterior cingulate gyrus, entorhinal cortex, perirhinal cortex, parahippocampal gyrus, isthmus of the cingulate gyrus, and temporal pole. Changes were also noted in the rostral middle frontal cortex, precentral gyrus, and suborbital sulcus.

Conclusions: These findings provide insight into the neural mechanisms associated with CM and MOH, highlighting distinct cortical alterations that may underlie these conditions.

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What headache types present to primary care in England? A retrospective cohort study of medical records

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[3]*Bollington, Adelphi Real World, United Kingdom*

Aim:

To understand headache types presenting to primary care in England.

Methods:

A retrospective cohort study using the Clinical Practice Research Datalink Aurum was conducted. Adults aged ≥18-years were indexed into the study on the first observed migraine or headache diagnosis between 19 September 2012 to 1 May 2023. Migraine and headache groups were mutually exclusive.

Prodromal/postdromal symptoms of migraine and potential misdiagnoses were defined using coded events in the 1-year prior to index diagnosis.

Results:

N=476,191 and 1,058,616 adults with migraine or headache were included, respectively – 78.0% and 63.1% female, mean (SD) age 42.1 (15.6) and 47.1 (17.9) years.

Headache and migraine groups experienced similar symptoms with depressed/low mood, dizziness, neck/muscle pain and fatigue being the most common.

Primary headache disorders (including migraine) comprised 39.5% of the cohort, secondary headache comprised 3.4% and the majority of headache was undifferentiated (57.1%). Nearly all people with an undifferentiated headache diagnosis remained without further headache diagnosis in the 1-year after diagnosis (99.9%).

A high proportion of the headache group had a potential misdiagnosis: neck pain (21.5%), sinusitis (20.6%), labyrinthitis (5.0%), transient ischaemic attack (4.6%).

Conclusions:

This study described headache types presenting to primary care in England. While symptom profiles were similar between groups, most patients with headache were diagnosed with undifferentiated headache and nearly all with undifferentiated headache did not receive a definitive diagnosis within 1-year. A high proportion of those with a headache diagnosis had features suggestive of migraine. Further research will understand socioeconomic disparities in healthcare utilisation in both groups.

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A rare presentation: case study of spontaneous intracranial hypotension

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Background:

Spontaneous intracranial hypotension (SIH) is a rare but significant cause of new onset daily persistent headaches, yet it remains underrecognized. Misdiagnosing this condition can lead to serious consequences, although magnetic resonance imaging has significantly facilitated the diagnosis.

Case history:

We describe a case of 36-year-old male with a one-month history of severe disabling orthostatic positional headaches accompanied by persistent nausea, dizziness, tinnitus, neck stiffness and clinically positive meningeal signs. Initial brain MRI revealed diffuse pachymeningeal thickening and enhancement, along with a 9 mm downward displacement of the brainstem and cerebellar tonsils, raising suspicion of intracranial hypotension. An MRI of the brain and spine with contrast did not identify the source of the cerebrospinal fluid leak. Therefore, a follow-up 3T spinal MRI with myelography was performed, which revealed two dural tears one of which inactive at the moment (spontaneously closed). Additionally, there was a central disc protrusion at L5/S1 and a focal protrusion with an annular tear and right foraminal compression at L4/L5. The diagnosis of idiopathic spontaneous intracranial hypotension type I was confirmed. Due to the spontaneous improvement of symptoms, a non-targeted epidural blood patch was not indicated, and conservative management was continued. Follow-up neuroimaging results were normal.

Conclusion:

This case emphasizes the importance of recognizing spontaneous intracranial hypotension and using serial and multimodal neuroimaging techniques for accurate diagnosis and management to prevent further complications, including brain sagging, dementia, ataxia, and cerebral venous thrombosis as well unnecessary and risky diagnostic procedures.

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Prevalence and Prognostic Factors of Post-SAH Headache: An 18-Month Cohort Study

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Advancements in diagnosis and multidisciplinary care have reduced Subarachnoid hemorrhage (SAH)-related mortality. However long-term complications such as post-SAH headache (PSH), cognitive dysfunction, and emotional disturbances significantly diminish quality of life. Objective: This study aims to evaluate the prevalence, characteristics, and prognostic factors of chronic PSH over an 18-month follow-up in a cohort of 47 patients. Methods: A prospective observational study was undertaken on 47 patients diagnosed with chronic PSH. Data collection encompassed demographic factors, acute-phase complications, and long-term cognitive and emotional disturbances. The data analysis was performed using the statistical software SPSS 25.0 (Statistical Package for Social Sciences). A p-value of ≤ 0.05 was considered statistically significant. Fisher grade and vasospasm severity were analyzed for their correlation with PSH using logistic regression and Pearson correlation. Results: The prevalence of PSH declined from 55.3% at 3 months to 25.5% at 18 months. Chronic PSH was significantly associated with cognitive dysfunction ($p=0.019$) and emotional disturbances ($p=0.023$). A strong positive correlation ($r=0.72$) was found between vasospasm severity and PSH likelihood, though non-linear patterns suggest additional influencing factors. Fisher grade severity predicted a 30% risk of developing chronic PSH. Conclusions: Chronic PSH significantly affects the quality of life of SAH survivors. Prognostic factors, including Fisher grade and vasospasm severity, can guide customized management strategies. Long-term monitoring and personalized therapeutic interventions are critical for improving patient outcomes and addressing chronic complications effectively.

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Prevalence and Prognostic Factors of Post-SAH Headache: An 18-Month Cohort Study

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Effects of Keto Diet in chronic migraine Effects of Keto Diet in chronic migraine

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Nutrition is widely known as one of the important environmental factors that interferes with the course of migraine. Migraineurs are sensitive to certain foods, also to the timing and amount of them. The mechanism through which nutrition could impact to the course of migraine is probably related with the decrease of the inflammation.

In a prospective study, during three-month period we enrolled 23 patients with migraine being being diagnosed as chronic migraine based on the ICHD-3 criteria, between 18 and 65 years-old, most of them females (69%). All participants started eating keto diet with 3:1 ratio of total fat combined with carbohydrates and protein. We evaluated patient in nutrition and neurological point of view. We observed a reduction of frequency of monthly headaches (12.8 ± 9.2 vs. 6.8 ± 8.5 p 0.001), frequency (17.2 ± 8.3 vs. 8.7 ± 6.2; p 0.001) and duration (23.4 ± 14.32 vs. 8.2 ± 11.3; p 0.001) and use of acute medications (10.2 ± 9.26 vs. 4.81 ± 7.87; p = 0.001). Also is seen reduction of weight (75.4 ± 14.3 vs. 67.2 ± 11.5; p 0.001), BMI (27.8 ± 5.9 vs. 22.4 ± 8.5; p 0.001), body fat mass (29.6 ± 13.3 vs. 21.2 ± 9.74; p 0.001).

Conclusions: With ketogenic diet was seen an improvement of headache frequency, intensity, and duration in patients with chronic migraine. Ketogenic diet may be considered an effective non-pharmacological intervention for migraine and also with positive outcomes on body composition.

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Hydrocephalus, whether apoplectiform onset is possible? Case report

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Hydrocephalus is a condition of expansion of the ventricles of the brain, a consequence of previously or currently increased pressure in the central nervous system, which is caused by an excessive amount of cerebrospinal fluid. The causes are different, and at the cause of all of them is a disorder of excessive secretion, accumulation and normal swelling of the cerebrospinal fluid.

When this process is altered or disrupted for some reason, cerebrospinal fluid accumulates causing hydrocephalus and damage to healthy brain tissue.

Obstructive hydrocephalus occurs due to obstruction of the outflow of cerebrospinal fluid, and the most common reasons for it are: tumors, the existence of scar tissue in the brain, congenital anomalies, thrombosis of the upper sagittal sinus.

Symptoms develop gradually, the most common are headaches, nausea, vomiting, changes in vision, gait disorder .

A fifty-year-old man comes to the Emergency Center for examintion due to a sudden headache the day before that does not go away with analgesics. Nausea,headache and vomiting occur. There are no deviations from normal in the neurological findings.

Head scan shows a tumor in the third cerebral ventricle corresponding to an ependymoma and obstructive hydrocephalus.

The patient was referred to a neurosurgeon

After the installation of the ventriculoperitoneal shunt, in good general condition, and with "satisfactory" findings on the brain scan, the patient was discharged home.

The literature describes cases of sudden changes of consciousness leading to coma, due to the sudden movement of the tumor, and the sudden development of hydrocephalus.

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Evaluation of Acute Headache in a General Hospital: Red Flags and Practical Challenges – A Retrospective Review from Emergency Department "Dr. Ivo Pedišić Sisak"

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Introduction:
Headache is a frequent complaint in emergency departments (ED), ranging from benign migraines to life-threatening conditions such as subarachnoid hemorrhage. Differentiating these requires a structured approach to avoid overdiagnosis or missed diagnoses.

Objective:
To propose a clinical algorithm for evaluating acute headaches in resource-limited settings like general hospitals, where challenges include limited diagnostic services, understaffing, and restricted imaging access. We emphasize identifying red flags and optimizing diagnostics within these limitations.

Methods:
A retrospective review of 441 headache cases in a general hospital ED over one year identified 189 cases meeting inclusion criteria: adult patients (≥18 years) with non-traumatic headache as the primary complaint and complete clinical data. Exclusion criteria included cervicocephalic syndrome, incomplete records, or other established diagnoses. A framework emphasizing red flags (e.g., sudden onset, neurological deficits, intracranial pressure symptoms) was used to identify life-threatening conditions like hemorrhages, tumors, ischemia, and severe infections.

Results:
Of the 189 cases, approximately 70% were classified as primary headaches, with 20% attributed to migraines and 50% to tension-type headaches. The remaining 30% represented secondary headaches, encompassing hemorrhages (10%), tumors (8%), ischemic stroke (5%), and meningitis (2%). Adherence to the proposed algorithm resulted in an estimated 23% reduction in unnecessary imaging, without compromising diagnostic accuracy or patient safety.

Conclusion:
A structured diagnostic approach enhances efficiency and safety in headache management, particularly in resource-limited settings. Limitations include the retrospective design, single-hospital focus, and reliance on clinical data, which may affect generalizability. Future prospective studies are needed to refine these findings.

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Idiopathic intracranial hypertension - from headache onset to diagnosis: case report

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Introduction: Idiopathic intracranial hypertension (IIH), also known as pseudotumor cerebri, is a rare condition, associated with increased intracranial pressure, with no obvious detectable cause and unknown pathogenesis. The condition is more common in women, as female gender, obesity and some medications (e.g. oral contraceptives) are recognised as risk factors. The main symptoms are severe headache, vision disturbances and vision loss, nausea, vommiting, tinnitus. Diagnosis is based on clinical symptoms, increases opening pressure on lumbar puncture and several MRI findings.

Case presentation: We present a 24-year-old overweight female patient with sudden onset of constant, severe, generalised headache, accompanied by nausea and followed 3 days later by blurred vision, reduced visual acuity and bilateral papilledema. CT scan and venography found no abnormalities, but MRI scan detected an empty sella sign and lumbar puncture revealed increased opening pressure (around 40-45cm H2O) with normal liquor protein, cells and glucose. A more detailed patient's history revealed that she had been prescribed dydrogesteron (a synthetic progesterone), which had been discontinued the day before the onset of her symptoms. After reaching a definite diagnosis, she underwent surgery for a ventriculo-peritoneal shunt placement and subsequently there was significant improvement, regarding her headache and visual acuity.

Conclusion: This case emphasised the necessity of including IIH as a deferential diagnosis in cases of sudden headache in women with several risk factors for IIH and the importance to act quickly in order to preserve the patient's vision.

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Acute communicating hydrocephalus and vestibular schwannoma- a case report

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The acoustic nerve tumor is a benign growth located along the course of the vestibulocochlear nerve, originating from Schwann cells, hence its name schwannoma. It is typically characterized by a unilateral location and slow growth. Symptoms vary depending on the size of the tumor and its potential mass effect. One common observation is the coexistence of communicating hydrocephalus. As the tumor grows gradually, ventricular system decompensation may occur, leading to the development of hydrocephalus with signs of increased intracranial pressure. A case is presented of a 40-year-old woman who experienced headaches in the occipital region and visual disturbances in the form of blurred vision, which began two weeks before she was admitted to the hospital. In addition, the patient complained of right limb muscle weakness, balance problems, right ear hearing loss and issues with concentration and memory over the past several months. A magnetic resonance imaging (MRI) of the head with contrast revealed signs of communicating hydrocephalus, with an acute angle of the corpus callosum measuring 46 degrees and signs of intracranial hypertension. A focal lesion was found in the right cerebellopontine angle, consistent with an acoustic neuroma of the right vestibulocochlear nerve. The patient was qualified for ventriculoperitoneal shunt implantation, which resulted in satisfactory short- and long-term clinical outcomes.

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Motor Neuron Disease

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Analysis of C9orf72 repeat expansions in Georgian patients with Amyotrophic lateral sclerosis (ALS)

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Background: Amyotrophic lateral sclerosis (ALS) is a fatal progressive neurodegenerative disorder that affects the upper and lower motor neurons. Several genetic risk factors have been identified in the past decade with a hexanucleotide repeat expansion in the C9orf72 gene being the most significant. However, the presence of C9orf72 repeat expansion has not been examined in the Transcaucasian region, therefore we aimed to analyze its frequency in Georgian patients with ALS.

Methods: We included 64 self-reported Georgian patients with ALS from different parts of the country, fulfilling the Gold Coast criteria. To investigate the presence of an expanded GGGGCC hexanucleotide repeat in the non-coding region of the C9orf72 gene, we performed Repeat-Primed PCR (RP-PCR).

Results: In total, 64 sporadic and two familial ALS cases were identified. Patients were aged 26 to 84 years with a mean age of 58.3 years at disease onset. Bulbar onset was observed in 21.88%, upper limb onset in 34.38%, and lower limb onset in 43.75% of the patients. Frontotemporal dementia (FTD) fulfilling the Strong criteria was diagnosed in seven patients (10.94%). C9orf72 repeat expansion was detected in only one case using RP-PCR; the patient had a family history of dementia.

Conclusions: Our results indicate that C9orf72 hexanucleotide expansion does not belong to the major genetic risk factor of ALS in Georgian patients. Further genetic studies in a bigger study population are needed to reveal the genetic causes of ALS in the Transcaucasian population.

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From Amyotrophic Lateral Sclerosis to Polyneuropathy: A Nerve-Wracking Relationship

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Introduction: Amyotrophic lateral sclerosis(ALS) is a devastating neurodegenerative condition of the motor neurons affecting around 4.5 people in 100,000. Chronic polyneuropathy is quite common in the general population, with a prevalence of up to 7%. Although ALS and axonal polyneuropathy can coexist without a causal relationship, the possibility of overlapping risk factors and shared molecular mechanisms was suggested by recent studies.

Methods: We conducted a cross-sectional study on the electronic medical record database at Colentina Clinical Hospital, a tertiary referral centre for ALS in Romania. We screened the available records that had G12.2 as the main ICD-10 diagnosis (i.e., motor neurone disease), up to December 2024. We included data from patients meeting criteria for ALS for which the result of at least one electroneuromyographic study was available.

Results: Data from 50 patients matched the inclusion criteria: 29 males and 21 females; mean age 59.7 years. Chronic axonal polyneuropathy was documented in 7 patients (14%) – sensory-motor in 6, sensory in 1. Of these, 4 patients had other possible explanations for their polyneuropathy (i.e., diabetes mellitus, toxic/nutritional), while 3 patients had no other possible explanation, 1 with flail arm onset, 1 with flail leg onset, and the third with a monogenic form. None of the patients had demyelinating polyneuropathy.

Conclusions: Three out of the 50 patients included in the study had unexplained chronic axonal polyneuropathy. Chronic axonal polyneuropathy could be part of the ALS disease spectrum. Understanding the link between these pathologies could open new directions in research and treatment.

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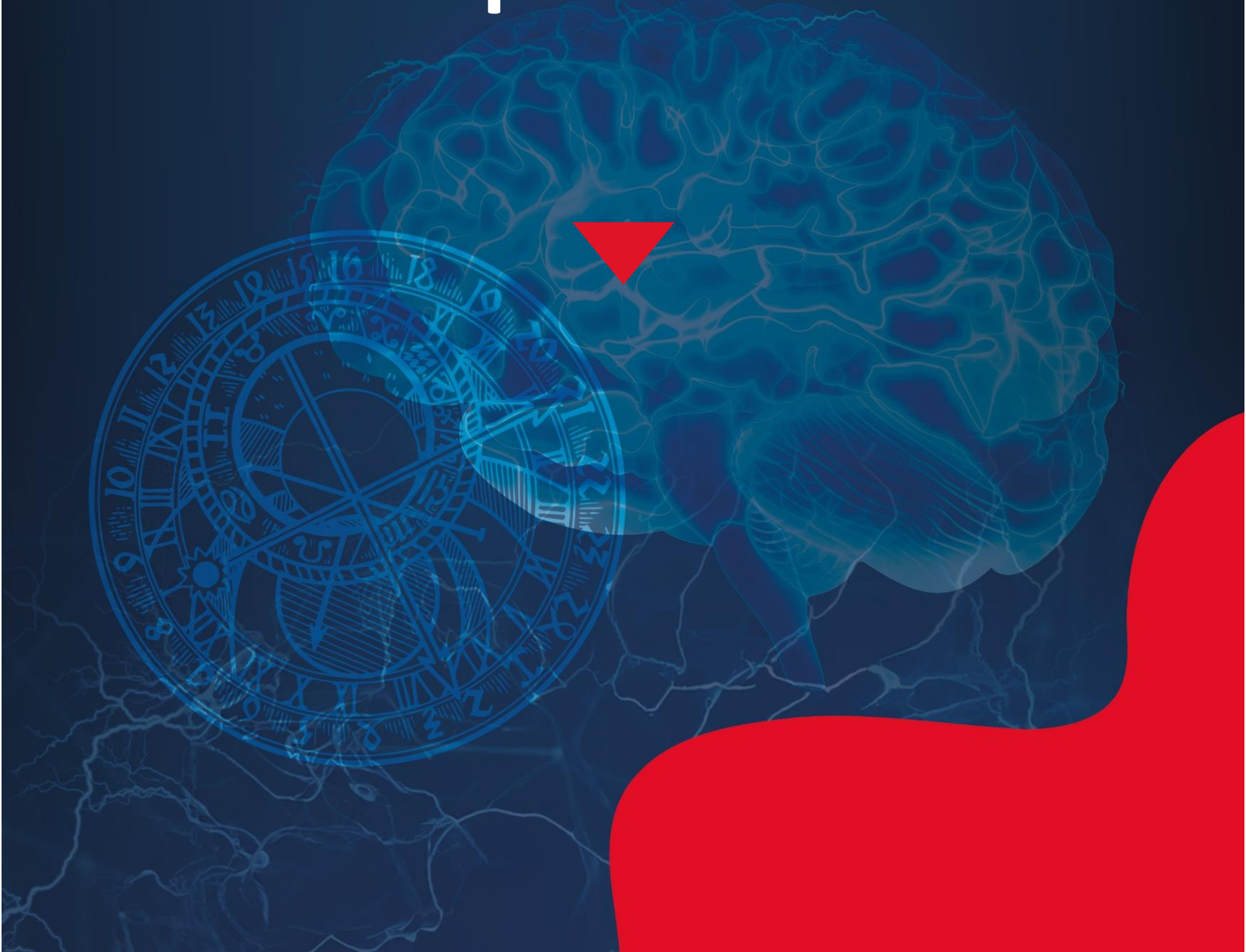
Multiple Sclerosis



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Exploratory MRI Outcomes and Plasma NfL Levels in Frexalimab-Treated Participants with Relapsing Multiple Sclerosis: Week 48 Results from the Phase 2 Open-Label Extension

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Introduction: Frexalimab, a second-generation anti-CD40L monoclonal antibody, inhibits the CD40/CD40L pathway that regulates adaptive and innate immunity. In a phase 2 trial (NCT04879628) for relapsing multiple sclerosis (RMS), frexalimab rapidly reduced new gadolinium-enhancing T1-lesions, but less is known about its effects on biomarkers of chronic neuroinflammation and neurodegeneration.

OBJECTIVES: Report exploratory MRI outcomes and changes in plasma neurofilament light chain (NfL) at Week (W) 48 in the phase 2 open-label-extension (OLE).

Methods: Participants were randomised to frexalimab$_{1200/\text{intravenous (IV)}}$ (n=52), frexalimab$_{300/\text{subcutaneous (SC)}}$ (n=51), or matching placebo (placebo$_{IV}$: n=12; placebo$_{SC}$: n=14). Participants receiving placebos switched to respective frexalimab at W12 and entered OLE. Exploratory assessments included paramagnetic rim lesions (PRLs), new T1-hypointense lesions, and NfL levels.

Results: 125/129 participants completed double-blind period and entered OLE; 112 (87%) continued the study as of 19-September-2023 (W48 cut-off). Mean baseline age±SD was 36.6±9.4 years; 66% women. At baseline, 19/46 (41%) of participants at sites with sufficient imaging capability had ≥1 PRLs. New PRLs were detected in frexalimab$_{300/SC}$ arms between W8 and W20, whereas no new PRLs were detected from baseline to W48 in frexalimab$_{1200/IV}$ arms. New T1-hypointense lesions (mean±SD) were low at W48: frexalimab$_{1200/IV}$, 0.1±0.4; frexalimab$_{300/SC}$, 0.8±1.6; placebo$_{IV}$/frexalimab$_{1200/IV}$, 0.0±0.0; placebo$_{SC}$/frexalimab$_{300/SC}$, 0.6±1.0. At W48, NfL levels (geometric mean±SD) were: frexalimab$_{1200/IV}$, 6.7±2.0; frexalimab$_{300/SC}$, 8.1±1.7; placebo$_{IV}$/frexalimab$_{1200/IV}$, 9.6±1.7; and placebo$_{SC}$/frexalimab$_{300/SC}$, 7.8±2.1 pg/ml, corresponding to 41%, 35%, 24%, and 33% reductions from baseline, respectively.

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Safety and Efficacy of Frexalimab in the Treatment of Relapsing Multiple Sclerosis: 18-Month Results from the Phase 2 Open-Label Extension

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Introduction: Frexalimab, a second-generation anti-CD40L antibody, blocks the CD40/CD40L pathway that regulates adaptive and innate immunity. In a phase-2 trial for relapsing multiple sclerosis (RMS; NCT04879628), frexalimab was well-tolerated and efficacious at reducing disease activity. Frexalimab 1200-mg intravenous (IV) every-4-weeks (q4w) decreased new gadolinium-enhancing T1-lesions by 89% vs placebo at W12. Treatment effect was sustained over W48 in open-label extension (OLE).

Objectives: Report safety and efficacy of frexalimab at W72 (18-months).

Methods: Participants were randomized (4:4:1:1) to receive 1200-mg IV q4w or 300-mg subcutaneous (SC) q2w doses of frexalimab or matching placebo. After W12, participants receiving placebos switched to respective frexalimab and entered OLE. During OLE, SC dose was increased to 1800-mg q4w to achieve a similar exposure as with the 1200-mg q4w IV dose; 7/57 participants had their W72 MRI after receiving high-dose. Key endpoints: safety and efficacy (number of gadolinium-enhancing T1-lesions and new/enlarging T2-lesions).

Results: 125/129 participants completed double-blind period and entered OLE; 111 (89%) had ongoing treatment as of 2-Feb-2024 (W72 cut-off). At W72, number of gadolinium-enhancing T1-lesions (mean±SD) remained low: frexalimab$_{IV}$, 0.1±0.4; frexalimab$_{SC}$, 0.4±0.9; placebo$_{IV}$/frexalimab$_{IV}$, 0.0±0.0; placebo$_{SC}$/frexalimab$_{SC}$, 0.2±0.4. New/enlarging T2-lesions and T2-lesion volume change remained low through W72. No new safety signals were observed; most common adverse events observed during OLE until W72 cut-off were nasopharyngitis (13%), COVID-19 (12%), and headache (11%).

Conclusions: Frexalimab continues to show favourable safety and sustained reduction in disease activity in RMS participants assessed by MRI through 18-months, supporting its further development in phase-3 MS trials as a high-efficacy, non-lymphocyte-depleting therapy.

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Diagnostic Age of Patients with Multiple Sclerosis in Azerbaijan: A Clinical and Epidemiological Study

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Introduction: Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system, characterized by inflammation and an unknown cause. MS most commonly affects individuals aged 20–40, with a female-to-male ratio ranging from 2:1 to 3:1, depending on the region. **The aim of this study** was to analyze the diagnostic age of MS patients in Azerbaijan.

Materials and Methods: This study analyzed data from 1,796 MS patients recorded under the "State Program on Measures of Treatment, Prevention, and Control of MS" over a ten-year period (2013–2022). Patients were grouped by 10-year diagnostic age intervals, and their sex, clinical course, residency, and diagnostic delay were evaluated.

Results and Discussion: Of the patients, 65.7% were female, and 34.3% were male, with an average diagnostic age of 34.9±8.9 years (range: 11–66). MS diagnoses were less prevalent in the 20, 50–59, and ≥60 age groups. The average diagnostic delay was 5.2±4.8 years. The highest proportion of diagnoses occurred in the 30–39 age group (39.15% women; 38.80% men). Women were more frequently diagnosed across all age groups, with the greatest disparity observed in those ≥60 (female-to-male ratio of 7:1). Relapsing-remitting MS was the predominant type in patients 60 (48.8%–88.6%), whereas secondary progressive MS was significantly more common in those ≥60 (75.0%, P0.001).

Conclusion: MS is most frequently diagnosed between the ages of 20–49 in Azerbaijan. Younger patients predominantly present with relapsing-remitting MS, while older individuals have a higher prevalence of secondary progressive MS.

Keywords: multiple sclerosis, 10-year age groups, age at diagnosis, clinical course.

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Lateral Ventricle Volume is associated with disease severity in Pediatric Multiple Sclerosis.

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Background: Although brain volume loss and its involvement in patient deterioration have been established, the effects of changes in the volume of the brain lateral ventricles in pediatric patients have yet to be thoroughly examined.

Aim: The purpose of this study was to examine changes in the lateral ventricular volume and its correlation with disease severity in POMS

Methods: Brain MRI performed at baseline and 3 years follow up were analyzed in POMS. The scans were segmented and quantified for volume using semiautomatic software. The POMS lateral ventricle volumes were matched to age and sex matched healthy subjects.

Results: Sixty six patients, (39 females) with mean ± SE age at onset 13.8 ± 0.4 years, baseline median Expanded Disability Status Scale (EDSS) score of 3.0 , disease duration of 8.1±0.5 years . After 3 years follow up the median EDSS were 1.0 (IQR 1.0-2.0) . At disease onset, the lower levels of lateral ventricle volume was associated with higher EDSS scores (p=0.05), that could be explained by more exudative inflammation in patients brains leading to reducing of ventricle volumes. In the opposite, after 3 years of the follow up, higher lateral ventricle volumes were now associated with higher EDSS scores (p=0.002), probably as it associated with initiation of neurodegeneration and neuronal loss.

Conclusion: Lateral ventricle volume in POMS associated with higher EDSS at onset and disease severity at 3 years follow up. This able as to follow patients deterioration and disease progression by conventional MRI observations, already in the onset and early disease progression.

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Tau in Multiple Sclerosis: Mediator or Bystander in Disease Progression?

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Introduction: Multiple Sclerosis (MS) is a neurological disorder characterized by inflammatory and neurodegenerative mechanisms. While disease-modifying therapies effectively control inflammation in relapsing-remitting MS, their limited impact on progressive MS highlights a critical gap in addressing neurodegeneration. Emerging evidence implicates tau, a protein traditionally associated with Alzheimer's disease, in MS. This raises the question: is tau merely a bystander in MS, or does it play an active role in driving neurodegeneration?

Methods: Utilizing specialized "biosensor" cell systems to detect and quantify tau seeds in brain tissues, we recently tested for and detected tau seeding in frozen brain tissue of 6/8 subjects with multiple sclerosis. Then, a critical review of literature was conducted, analyzing findings from rodent models, human brain tissue, cerebrospinal fluid studies, and PET imaging. The review explored the relationship between inflammation and degeneration in the context of tau pathology.
Results: Based on the review of existing studies, abnormal tau is present in MS brains, with insoluble tau aggregates emerging in progressed disease. Tau seeds have been identified in border zones of lesions, but their role in MS pathophysiology remains unclear. Tau may act as an acute-phase protein in early inflammation, undergoing post-translational modifications and aggregation, potentially driving neurodegeneration. Immunoprecipitation studies suggest tau aggregates in MS exhibit distinct conformations compared to Alzheimer's disease.

Conclusion: Evidence suggests tau as a mediator in MS progression - but challenges remain. These include the lack of reliable animal models, limited brain tissue access, and unvalidated biomarkers. Overcoming these barriers could enable novel therapeutic strategies targeting tau aggregation or modulating inflammatory pathways to mitigate neurodegeneration in progressive MS.

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Case report: Therapeutic controversy: patient with sudden onset of NMOSD treated with rtPA

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The case presents a 38-year-old patient who developed sudden massive paresis of the left limbs. Based on the dynamics of symptom development and the results of a head CT scan, an ischemic stroke was suspected and the patient was qualified for rtPA treatment (in the hospital where the patient was diagnosed, it was not possible to urgently perform an MRI). On the next day, the patient developed tetraparesis with persistent hiccups and nausea. MRI of the head and cervical spinal cord revealed a long-segment T2 hyperintense lesion from the level of the medulla oblongata to the level of C6 Gd(+) and with signs of spinal edema. Additionally, area postrema involvement was found. No AQP4-IgG or anti-MOG antibodies were detected, but visual evoked potential testing revealed bilateral demyelinating damage to the visual pathway. Treatment with methylprednisolone infusions was performed, 5 plasmaphereses were performed, followed by immunoglobulin infusions, resulting in clinical improvement and the diagnosis of AQP4-IgG-seronegative NMOSD was made.

Conclusions: The rtPA treatment used in a patient with acute onset of NMOSD did not lead to bleeding complications. The use of rtPA in the course of acute ischemic stroke in patients diagnosed with NMOSD may be a safe form of treatment. This is probably the first described case of a patient who was treated with rtPA in the course of NMOSD.

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Trigeminal neuralgia in multiple sclerosis – case series

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Introduction

Trigeminal neuralgia, characterized by intense, stabbing pain attacks, may result from demyelinating lesions in the pons or spinal trigeminal nucleus in MS. This study examines MS patients with trigeminal neuralgia, analyzing nuances to refine patient care strategies.

Methods

We retrospectively examined five cases of MS patients with trigeminal neuralgia. For each case, we reviewed medical records to determine the onset times of MS and trigeminal neuralgia, as well as the medications and interventions for trigeminal neuralgia. Brain MRI images were analyzed to identify demyelinating lesions near the trigeminal ganglion.

Results

Among the patients studied, four were female and one male, with ages ranging from 44 to 48 years. Three had relapsing-remitting MS (with EDSS scores between 1 and 2), while two had secondary progressive MS (both with EDSS = 6.5), with disease onset occurring between the ages of 29 and 37. Trigeminal neuralgia typically developed approximately 9.6 years after the onset of MS. Imaging revealed pontine lesions in three patients, vascular-nerve conflict in one, and no significant lesions in another. Initial drug treatments were attempted for all patients, but two showed no response. As a result, interventions such as Gasser ganglion ablation or microvascular decompression were performed, but these did not lead to substantial symptom improvement. One patient relapsed after 4 months, while the other showed no noticeable change.

Conclusions

In summary, this case series underscores the link between multiple sclerosis and trigeminal neuralgia, emphasizing diagnostic complexities and the need for a personalized, multidisciplinary approach.

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Lifestyle Interventions in Depressive People with Multiple Sclerosis: a Review

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Depression is considered to be one of the most common comorbidities in people with multiple sclerosis. It is connected to the reduction in the quality of life of people in multiple sclerosis, and an increase in health care expenses due to an increased health system usage.
We conducted a literature review in order to summarize the publications published in the last five years concerning lifestyle interventions that might be used to reduce depressive symptoms.
Regular physical activity shows a positive impact on depression levels in people with multiple sclerosis: home-based exercises as well as physiotherapy should be encouraged.
Ketogenic diet reduces depression levels, improves quality of life, cognitive and motor skills of people with multiple sclerosis, yet it should only be undertaken under medical supervision as it could possibly lead to unwanted side-effects after a longer period of time.
A reduction in depressive symptoms can also be achieved through psychological education, mindfulness-based programs, cognitive and dialectical behavior therapy.
Screening for depressive symptoms in people with multiple sclerosis should be made regularly. Next to undertaking further pharmacological steps upon eventual positive screening, neurologists should encourage people with multiple sclerosis in making lifestyle changes which could be helpful reducing depressive symptoms.

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Assessing Nutritional Knowledge and the Quality of Dietary Recommendations for Patients with Multiple Sclerosis in Ukraine: a Mixed-Methods Study

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Introduction: Nutrition knowledge is a potential tool for improving disease management in multiple sclerosis (MS). This study evaluates patient satisfaction with dietary advice and explores the need for tailored educational materials.

Methods: A sequential explanatory mixed-methods design was used. Quantitative data were collected through structured online questionnaires from MS patients receiving treatment at Kyiv City Clinical Hospital №4 in Ukraine between November 2024 to January 2025, and descriptive statistics were calculated. Semi-structured interviews were then conducted until thematic saturation was reached.

Results: A total of 59 patients were invited to participate in the survey, with 7 declining to participate. The median age was 36 (IQR: 29-42). The group included 38 (65,4%) inpatient and 14 (34,6%) outpatient participants, with 65,4% being female. Patients were categorized as having relapsing-remitting (86.5%), primary progressive (9.6%), secondary progressive (3.9%) forms of MS. A majority (70.6%) considered nutrition recommendations important, while 49% initiated the primary dialogue about nutrition with physicians, and 67.4% sought information online. Satisfaction with online resources averaged 3.7/5 (n=30), compared to 3.6/5 (n=23) for information provided by physicians. Interviews were conducted with seven patients. Three major themes were identified: insufficient evidence-based dietary recommendations, the need for personalized guidance and gaps between recommendations between different physicians.

Conclusion: This study indicates moderate satisfaction with dietary information from online and physicians-provided sources, underscoring a necessity for improvement. Patients with MS value nutrition in disease management and express interest in receiving evidence-based guidance, highlighting the need for better educational materials.

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Why navigated transcranial magnetic stimulation is not used in clinical settings as an objective method for assessing motor disability in patients with multiple sclerosis?

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Although MRI has become the standard in diagnosing and monitoring patients with multiple sclerosis (MS), the evoked potentials (EP) (motor EP -MEP, somatosensory EP-SEP, and visual EP-VEP) for assessing functional integrity of motor and sensory pathways are unjustifiably considered less useful. MEP latency provides congruent information on the function of the corticospinal tract and is closely related to clinical EDSS score. A combination of two or all three EP modalities is significantly related to future EDSS scores over two to twenty years in CIS, RRMS, and PPMS. Recent studies point to MEP latency as the promising marker for an objective assessment and monitoring of motor disability in MS.

In the present study, navigated transcranial magnetic stimulator (nTMS) was used for mapping the corticospinal tract integrity for upper and lower extremity muscles as an additional tool to standard EDSS clinical assessment. The study will present several cases of PPMS and RRMS patients in whom nTMS was performed showing clear benefits in addition to standard EDSS evaluation. Ongoing clinical recommendations for MEP use in MS refer to the application of a magnetic stimulator connected to a standard EMG unit, and less to-line navigated TMS and electric-field navigated TMS implementations that could provide more precision in targeting and visualization of the primary motor cortices for single muscle representation.

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Efficacy and Safety of Inebilizumab Among Non-White Demographic Groups with Neuromyelitis Optica Spectrum Disorder: N-MOmentum Study Subgroup Analysis

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Background: There is a need for efficacy and safety information of disease modifying therapies on Neuromyelitis Optica Spectrum Disorder (NMOSD) in non-White demographic groups. Inebilizumab (INEB), an anti-CD19 B cell depleting antibody, is approved for the treatment of NMOSD in adults seropositive for aquaporin-4 antibody (AQP4+).

Methods: N-MOmentum (NCT02200770) was a double-blind, phase 2/3 trial that assessed the efficacy and safety of INEB in adults with NMOSD, with a 28-week randomized controlled period (RCP) (intravenous INEB 300 mg or placebo [PBO] on days-1 and 15) and an open-label period (OLP) of ≥2 years.

Results: Participants receiving INEB in the RCP were less likely to have an attack compared to PBO (Hazard Ratio[95%CI], p-value): Asian 0.20[0.06, 0.66], p=0.01; H/L 0.25[0.06, 1.01], p=0.05; B/AA 0.33[0.02, 5.31], p=0.44; White 0.27[0.11, 0.66], p=0.004. Expanded Disability Status Scale (EDSS) worsening from baseline to last RCP visit for participants receiving INEB vs PBO (Odds Ratio[95%CI], p-value): Asian 0.58[0.09, 3.63], p=0.56; H/L 0.50[0.09, 2.70], p=0.4; White 0.37[0.14, 0.95], p=0.04; and B/AA participants receiving INEB (0/15) did not experience EDSS worsening compared to 20% of PBO (1/5) participants. Participants who received any INEB during the study (combined RCP/OLP), the annualized attack rate [95% CI] was: Asian 0.10[0.05, 0.18]; H/L 0.07[0.04, 0.15]; B/AA 0.05[0.01, 0.33]; White 0.08[0.05, 0.13]. Among INEB participants, ≥1 investigational product-related treatment-emergent adverse event was reported: Asian(16/46); H/L(12/40); B/AA(12/19); White(48/120).

Conclusions: Non-White NMOSD participants receiving inebilizumab had improved outcomes when compared to placebo and were similar to White participants although evaluation of larger populations is needed to confirm these results.

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Impaired Cerebrospinal fluid circulation and cerebral lymphatic drainage in a rat model of chronic Hydrocephalus

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The cerebrospinal fluid (CSF) not only protects the brain but also maintains homeostasis by removing metabolic waste produced by brain activity. This study hypothesizes that chronic CSF circulatory dysfunction, such as normal pressure hydrocephalus (NPH), may be a critical condition in neurodegenerative diseases associated with metabolic waste accumulation. To investigate the glymphatic system and cerebral lymphatic drainage in a rat model of chronic hydrocephalus nduced by kaolin injection, we performed time-dependent evaluations of intraparenchymal injection of tracers or intra-cisterna magna, as well as intraventricular injection of Evans blue. The study systemically evaluated the dysfunction of CSF circulation and lymphatic drainage in the brain from various perspectives, including the glymphatic system, transependymal CSF flow, subarachnoid CSF flow, meningeal lymphatic drainage, and peripheral lymphatic drainage to deep cervical lymph nodes. The results indicated delayedglymphatic and cerebral lymphatic drainage in he kaolin-induced hydrocephalus model. Based on these findings, our research indicated that dysfunction of CSF circulation, as observed in conditions such as NPH, may act as an initiating or exacerbating factor in neurodegenerative diseases. This can lead to the accumulation of metabolic waste, as seen in Alzheimer`s disease. Our research can help identify risk factors and provide insight into the underlying pathophysiology of neurodegenerative diseases, which may lead to the development of novel therapeutic strategies.

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Spinocerebellar Ataxia Type 2 (SCA2) confirmed with memory impairment as the only clinical manifestation

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Spinocerebellar Ataxia Type 2 (SCA2) is an autosomal dominant disorder characterized by gait disturbances, limb ataxia, dysarthria, eye movement disorders, and neuropathy. In the later stages of the disease, extrapyramidal symptoms, along with dementia, may develop. The author reports a patient with a family history of spinocerebellar ataxia who exclusively complained of memory impairment, and was diagnosed with SCA2 through genetic testing.

A 56-year-old woman began to experience memory issues approximately 5 years ago. Around 4 years ago, she started having difficulty remembering dates and became disoriented, often getting lost on familiar routes. Her mother was diagnosed with spinocerebellar ataxia after experiencing symptoms such as hand tremors, muscle wasting, and difficulty walking at a young age. Neurological testing revealed cognitive impairments, including deficits in memory, attention, and executive functions (Table 1), but no significant physical signs of ataxia. Despite a normal brain MRI (Fig) and no clear clinical signs of SCA, genetic testing confirmed the diagnosis of SCA2 due to an abnormal CAG repeat expansion in the ATAXIN2 gene (Table 2).

This case highlights that cognitive decline in SCA2 can occur without prominent cerebellar motor symptoms, and emphasizes the importance of considering family history and performing genetic testing for accurate diagnosis, particularly when symptoms suggest conditions like early-onset Alzheimer`s. The article also discusses the broader impact of SCA on cognitive functions, including its association with dementia and memory impairment, and introduces the concept of cerebellar cognitive affective syndrome (CCAS), in which cerebellar dysfunction affects higher cortical functions.

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Exploring the link between neurodevelopmental vulnerabilities and neurodegenerative manifestations

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Primary progressive aphasia (PPA) is a clinical manifestation characterized by gradual decline in language functions secondary to neurodegenerative processes affecting language areas or networks in the brain. Two studies have found an association between the occupation of teaching and development of PPA (Jiskoot et al., 2024, Josephs et al., 2013). Two possible hypotheses have been proposed to explain this association. One, by nature of their occupation, teachers are sensitive to subtle changes in their verbal abilities, and the other that they are at risk for developing these disorders due to their frequent use of verbal and written communication (Josephs et al., 2013). Jiskoot et al (2024) refer to the latter as the "wear and tear hypothesis." In this presentation, I explore the possibility that an extraneous variable could have explained the association between the occupation of teaching and development of PPA. Specifically, I propose an alternative hypothesis that teachers who have a neurodevelopmental vulnerability (e.g., learning disability) are the ones at risk for developing PPA. This hypothesis is primarily derived from the finding that there is a high frequency of learning disability in patients with PPA and their first-degree relatives (e.g., Rogalski et al., 2008). I will discuss the clinical and theoretical implications of exploring this alternative hypothesis.

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Peripheral neuromotor system disorders in Alzheimer`s disease

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Degenerative diseases with cognitive dysfunction and peripheral neuromotor system abnormalities predominate in older people. We decided to study the function of peripheral nerves in Alzheimer`s patients to identify a correlation between these two processes and the potential use of peripheral lesions as biomarkers for Alzheimer`s disease.

Material and methods. 10 patients with mild cognitive dysfunction (5 men and 5 women), 4 patients with Alzheimer`s disease (2 men and 2 women) and 10 healthy people (5 women and 5 men) were examined. The age of all patients ranged from 60 to 80 years. Alzheimer`s disease and mild cognitive dysfunction were diagnosed using MoCA. Sensor and motor fibers of the n.medianus, n. peroneus and n. tibialis, n. suralis and n. peroneus superficialis were examined. Nerve conduction velocity, amplitude and latency of S- and M-responses were studied. The ENMG study was performed using a Keypoint electromyograph from Metronics.

Result: The slowing of conduction velocities in the n.medianus and n.peroneus motor fibers was qualitatively greater in patients with Alzheimer`s disease than in those with mild cognitive dysfunction. In older adults without cognitive dysfunction, the nerve conduction velocities in the motor fibers of these two nerves were higher than in those with mild cognitive dysfunction persons.

Conclusion:It can be assumed that the rate of NCV decrease along motor fibers of peripheral nerves increases as cognitive function declines. Whether peripheral nerve function can be used as an early diagnostic marker for Alzheimer`s disease requires further elucidation, although it opens new avenues for future biomarker research.

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Wernicke's Encephalopathy: A Case Report of Alcohol-Related Thiamine Deficiency

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Wernicke's encephalopathy (WE) is a severe neurological disorder caused by thiamine deficiency, most commonly associated with chronic alcohol misuse. We present the case of a 63-year-old male with a history of prolonged alcohol dependence who acutely developed confusion, gait ataxia, and memory deficits after abrupt cessation of alcohol consumption.

Neurological examination revealed horizontal gaze palsy, severe ataxia, and disorientation. MRI demonstrated symmetrical T2 hyperintensities in the periaqueductal gray matter, mammillary bodies, and thalami, consistent with Wernicke's encephalopathy. Laboratory workup confirmed marked thiamine deficiency and microcytic anemia linked to chronic gastrointestinal bleeding.

The patient received high-dose intravenous thiamine, leading to partial improvement in gait stability and alertness. However, persistent amnestic symptoms reflected irreversible damage due to delayed intervention.

This case underscores the necessity of prompt recognition and treatment of thiamine deficiency in alcohol-dependent patients. Early thiamine administration remains the cornerstone of management to prevent irreversible neurodegeneration. Clinicians should maintain a high index of suspicion for WE in patients presenting with the classic triad of ophthalmoplegia, ataxia, and confusion, even if all features are not initially evident. This report highlights the preventable nature of WE and the critical role of early intervention in mitigating long-term morbidity.

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Sleep Disorders as Non Motor Symptoms in GBA parkinson`s patients in Albania

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Background: Parkinson`s disease (PD) is the second most common neurodegenerative movement disorder. The etiology of the disease is unknown, but number of monogenic forms for PD were described over the last 2 decades. More frequently are identified pathologic variants in GBA, LRRK2, SNCA,PARK2. Sleep disorders is also a significant characteristics of PD, as rapid eye movement sleep behavior disorder (RBD), restless legs syndrome (RLS), excessive daytime sleepiness (EDS), insomnia, obstructive sleep apnea (OSA) and circadian rhythm disturbances.

Methods: In the study are included 41 patients fullfill all criteria of Parkinson disease. These are divided into to groups. In the first group are included 9 patients carring mutations of GBA1 heterozigotes or compound heterozigote, 1 patient LRRK2 and in the second group are included 31 patients with PD without presence of GBA patologic variants.

Results: In the first group with 10 patients carring mutations of GBA heterozigotes or compound heterozigotes and 1 patient LRRK2 and second group 31 patients NMS. Sleep disorders RBD 30%, RLS 30%, EDS 20%, insomnia 10 % of all PD patients carring mutation of GBA, PD patient with mutation LRRK2 has RBD. In the second group 19 % has RBD, 16% has RLS, EDS 16 %, and insomnia 13%.

Conclusion: Sleep disorders, such as RBD, RLS, EDS and insomnia, are the most common non-motor feature of PD and often antedate PD, suggesting that sleep disorders are closely related to PD pathophysiology. Non motor symptoms are more prominent in GBA PD patients compared with PD patients

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Improvements in Pain and Disability Contribute to Improved Quality of Life After Inebilizumab Treatment in Attack-Free Neuromyelitis Optica Spectrum Disorder (NMOSD) Participants

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Background: Chronic pain and disability are enduring effects of NMOSD and contribute to decreased quality of life (QoL). Here we evaluated Pain and QoL improvement in attack-free, inebilizumab-treated participants over 3-years to determine improvements in non-attack related Pain and QoL.

Methods: N-MOmentum (NCT02200770) was a phase 2/3 trial in 230 participants (randomized 3:1, inebilizumab 300mg:placebo), with an open-label extension of ≥2 years. Year-over-year changes in pain (SF-36-Bodily-Pain-Score [BPS]), QoL (SF-36-physical-component-summary [PCS]), and disability (Expanded-Disability-Status-Scale [EDSS]) were assessed for significance using mixed linear models in participants who were attack-free with ≥3-years of inebilizumab. Sensitivity analysis was conducted in participants who were attack-free for ≥6 months prior to inebilizumab treatment to control for acute attack-related recovery.

Results: At Baseline, (36/95) participants reported an abnormal QoL score (SF36-PCS40), (32/36) of these participants reported increased pain (SF36-BPS40) and (18/36) reported significant disability (EDSS≥5). After 3-years of inebilizumab, QoL scores improved in (32/36) of attack-free participants with an abnormal baseline QoL score. (37/95) of participants had abnormal pain scores (SF36-BPS40) at baseline and improvements were reported in (29/37) p0.001 after 3-years of inebilizumab. SF36-PCS and BPS scores improved in participants with normal (≥40) baseline scores after 3-years of inebilizumab. Improvements in EDSS from baseline to 3-years of inebilizumab were observed in (40/91) of participants including (25/69) with less disability (5 EDSS) and (15/22) with greater disability (≥5 EDSS) at baseline. Results were consistent with the sensitivity analysis.

Conclusions: Year-over-year improvements in Pain, QoL, EDSS and FSS were observed in attack-free participants on inebilizumab and independent of acute attack-related recovery.

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Case of Myotonic Dystrophy type 1

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Introduction: Myotonic dystrophy (MD) is a type of muscular dystrophy, a group of genetic disorders that cause progressive muscle loss and weakness. In MD, muscles often fail to relax after contraction..

Case summary: The presented patient is a 30-year-old man with complaints of noticeable gait disturbance (foot drop), weakness in the distal parts of the upper and lower extremities, spasm during movement, difficulty starting movement.

Neurological status: Deformity of the chest - sunken sternum. The configuration of the spine is altered. The shoulders and scapulae are asymmetrical, muscle hypotrophy of the shoulder girdle, upper arm, forearm, lower leg (more on the left).

Gait is impaired, when walking, the right foot hangs down.

Muscle tone decreased. Muscle strength in the shoulder girdle is 5 points (proximally), in the shoulder flexors - 4 points, in the extensors of the hand - 2 points. Muscle strength in the proximal part of the lower extremities is 5 points, in the distal part 2-3 points. Percussion myotonic reactions are positive on both sides.

Reflexes from m. biceps and m. triceps is symmetrically decreased, periosteal reflexes are absent. Knee and Achilles reflexes are absent.

In the Romberg pose, he is stable, in the complicated Romberg pose - slight rocking. He performs the heel-knee test well. Coordination tests - minor disturbances.

Electromyography: the impulse conduction velocity in the motor nerves (ICVeff) is slow, the amplitude of the M-potentials is reduced. The values of ICVaff and S-potentials are normal. Needle EMG revealed positive waves at rest and "myotonic" discharges. The amplitude of the motor unit potensial (MUP) is reduced. Echocardiography: Segmental motor failure of the left ventricle.

Conclusion: Based on clinical and EMG data, the patient was diagnosed with myotonic dystrophy type 1 and received drug (tegretol, etc.) and physiotherapy treatment.

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Nonfluent/Agrammatic Primary Progressive Aphasia in the Context of Accelerated Post-COVID-19 Neurodegeneration: A Case Report

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Background: Primary Progressive Aphasia (PPA) is a rare neurodegenerative disorder characterized by progressive impairment in language, often linked to frontotemporal lobar degeneration (FTLD). The nonfluent/agrammatic variant (naPPA) is distinguished by effortful speech, agrammatism, and apraxia of speech. Viral infections, including COVID-19, may act as triggers or accelerators of neurodegeneration.

Case Presentation: A 56-year-old female presented with progressive speech and language impairment over 7–8 months. Several months before the appearance of cognitive symptoms she had confirmed COVID-19 infection two times. Initial symptoms included word-finding difficulty and sentence construction issues, progressing to severe deficits in speech production, reading, and writing. Due to these, it was impossible to conduct MMSE and MOCA tests. Neurological examination revealed slow, hypokinetic gait, diminished arm swing, ideomotor apraxia, amimic face, pseudobulbar affect, and dysphagia.

Investigations: EEG demonstrated paroxysmal activity in the left temporal lobe with rhythmic beta slowing. MRI revealed cortical atrophy in the left temporal and parietal lobes, with globus pallidus hypointensity, and mild chronic periventricular leukoencephalopathy. CSF analysis was unremarkable, excluding infectious and autoimmune causes.

Conclusion: In summary, this case highlights the clinical evolution and diagnostic challenges of naPPA, underscoring the importance of multimodal imaging and EEG in evaluation. The possible connection between COVID-19 and accelerated tauopathy calls for further investigation. Prompt diagnosis and a multidisciplinary strategy are essential for optimal patient management.

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Phase 3 Trial Designs Evaluating Riliprubart, a C1s-Complement Inhibitor, in Chronic Inflammatory Demyelinating Polyneuropathy

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Introduction: Standard-of-care (SoC) therapies for chronic inflammatory demyelinating polyneuropathy (CIDP) have variable efficacy and side-effects. Riliprubart, a first-in-class, humanized, IgG4-monoclonal antibody, selectively inhibits activated-C1s, and has convenient weekly subcutaneous administration. Phase 2 (NCT04658472) results indicated promising clinical benefits on functional disability, reduced neurofilament light chain-levels, and a favorable benefit:risk profile.

Aim: To present two Phase 3 trial designs evaluating riliprubart in high unmet-need CIDP subpopulations: participants refractory to SoC therapies, and responders to intravenous immunoglobulins (IVIg) with residual disability.

Methods: MOBILIZE ((NCT06290128), is a placebo-controlled trial initiated in SoC-refractory participants; VITALIZE (NCT06290141), is a double-dummy trial targeting IVIg-treated participants with residual disability (i.e., persistent Inflammatory Neuropathy Cause and Treatment [INCAT] score ≥2). Each trial consists of 48-week period: 24-week double-blinded period (Part-A), followed by an additional 24-week open-label period (Part-B). In Part-A, participants are randomized (1:1) to receive riliprubart or placebo (MOBILIZE; N~140), and riliprubart plus IVIg-placebo or IVIg plus riliprubart-placebo (VITALIZE; N~160). Sample sizes will be re-estimated based on pre-defined interim analysis during Part-A. Eligible adults with CIDP diagnosed based on 2021 EAN/PNS guidelines with INCAT score 2-9 (score 2 exclusively from legs) can be included. Primary endpoint is %-participants responding, defined as ≥1-point decrease from baseline in adjusted INCAT score at Week-24 (Part-A). Key secondary endpoints include change from baseline in additional disability/impairment measures (Part-A) and long-term safety (Part-B).

Results: Recruitment is ongoing for both trials.

Conclusions: Phase 3 trials aim to demonstrate riliprubart's efficacy and safety for CIDP, including participants with residual disability/refractory disease despite SoC therapies.

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Phase 2 Efficacy and Safety of Riliprubart, a C1s-Complement Inhibitor, in Chronic Inflammatory Demyelinating Polyneuropathy

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Introduction: Riliprubart, a first-in-class humanized IgG4-monoclonal antibody, selectively inhibits activated-C1s within the classical complement pathway.

Aim: To report efficacy and safety of riliprubart in chronic inflammatory demyelinating polyneuropathy (CIDP).

Methods: Global, multicentre, Phase-2, open-label trial (NCT04658472) evaluating riliprubart across three groups of participants with CIDP: Standard-of-care (SOC)-Treated, SOC-Refractory, and SOC-Naïve. Participants undergo 24-week treatment (Part-A), and 52-week Part-B (optional). Part-A primary endpoint for SOC-Treated is %-participants with relapse (≥1-point increase in adjusted Inflammatory Neuropathy Cause and Treatment [INCAT] disability score) after switching from SOC to riliprubart. For SOC-Refractory and SOC-Naïve, primary endpoint is %-participants with response (≥1-point decrease in adjusted INCAT score) from baseline up to 24-weeks. Part-B evaluates safety and efficacy durability based on % relapse-free participants (SOC-Treated) or with sustained-response (SOC-Refractory/Naïve). Exploratory endpoints include additional efficacy measures (INCAT, I-RODS, MRC-SS, grip-strength), change in total complement, and plasma neurofilament-light chain (NfL).

Results: As of May-2023, Part-A results from pre-specified interim-analysis show that 88% (N=22/25) SOC-Treated participants improved or remained stable (44%; N=11/25 improved), and 12% relapsed (N=3/25). For SOC-Refractory participants, 50% (N=9/18) responded to riliprubart. Clinically meaningful improvements were observed across secondary efficacy measures. Sustained inhibition of complement activity and reduction in NfL levels were observed. Treatment-emergent adverse events occurred in 60% (N=15/25) and 72% (N=13/18) of SOC-Treated and SOC-Refractory participants, respectively. Most frequent TEAEs were headache, fatigue, and nasopharyngitis. Available Part-A and Part-B data for all groups will be presented at the meeting.

Conclusions: Preliminary results demonstrate a favourable benefit:risk profile, supporting further investigation of riliprubart in Phase-3.

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Efficacy and Safety of Efgartigimod PH20 Subcutaneous in Chronic Inflammatory Demyelinating Polyneuropathy: Results of ADHERE/ADHERE+

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Introduction: Efgartigimod, a human immunoglobulin G (IgG)1 antibody Fc fragment, blocks the neonatal Fc receptor, decreasing IgG recycling and reducing pathogenic IgG autoantibody levels. This study aims to assess the efficacy and safety of efgartigimod PH20 subcutaneous (SC; coformulated with recombinant human hyaluronidase PH20) in chronic inflammatory demyelinating polyneuropathy (CIDP).

Methods: Participants with active CIDP (off treatment or on standard treatments withdrawn during run-in) enrolled in the multi-stage, double-blinded, placebo-controlled ADHERE trial (NCT04281472) and received once weekly (QW) efgartigimod PH20 SC 1000mg (stage A). Responders were randomized (1:1) to QW efgartigimod PH20 SC 1000mg or placebo (stage B). Participants with clinical deterioration in stage B or those who completed ADHERE could enter the ongoing, open-label extension ADHERE+ trial (NCT04280718; QW efgartigimod PH20 SC 1000mg). Primary outcomes were confirmed evidence of clinical improvement (ECI; stage A), relapse risk (stage B), and safety (ADHERE+).

Results: In stage A, 214/322 (66.5%) participants demonstrated confirmed ECI. In stage B, efgartigimod significantly reduced relapse risk (HR: 0.394 [95% CI 0.253–0.614]) vs placebo (P=0.00004); this reduction was observed regardless of prior CIDP therapy. 99% of eligible participants entered ADHERE+. The safety profile of efgartigimod was consistent over 137.42 total patient-years of follow-up for ADHERE+. Most treatment-emergent adverse events were mild/moderate; the incidence/severity did not increase in ADHERE+.

Conclusion: ADHERE demonstrated effectiveness of efgartigimod PH20 SC in reducing relapse risk in CIDP. The safety profile of efgartigimod PH20 SC was similar between ADHERE and ADHERE+ and was consistent with the previously demonstrated safety profile of efgartigimod.

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Distal weakness and paresthesia with facial diplegia: An uncommon variant of Guillain-Barre syndrome

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Background: Bilateral facial weakness with distal paresthesia (BFWdp) occurs in less than 1% of Guillain-Barré syndrome (GBS) cases. GBS can present as a distal acute demyelinating polyradiculoneuropathy, characterized by severe distal demyelination without radiculitis. We report a 63-year-old male with distal weakness, paresthesia, and facial diplegia. Case: A previously healthy 63-year-old male developed distal weakness, facial diplegia, and severe distal paresthesia, consistent with acute distal demyelinating sensorimotor polyneuropathy. Examination revealed bilateral facial paralysis, left partial oculomotor nerve palsy, reduced sensation in both distal limbs, and distal weakness. Proximal strength was minimally reduced. Cerebrospinal fluid showed albuminocytological dissociation, and ganglioside and anti-MAG antibodies were negative. Ultrasound revealed swelling of the median and ulnar nerves, while the sural, vagus, and brachial roots were normal. After intravenous immunoglobulin treatment, the patient improved. Two years later, the patient still had tingling in the hands and feet, but there was no recurrence or progression on NCS.

Discussion: The clinical and NCS findings suggest a mixed GBS phenotype, characterized by BFWdp and a distal phenotype. GBS can present with various manifestations and electrodiagnostic features, requiring serial NCS and clinical follow-up for a definitive diagnosis.

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Achievement of Minimal Symptom Expression in Participants Treated With Efgartigimod in ADAPT+ and ADAPT-SC+

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Introduction: Efgartigimod, a human immunoglobulin G (IgG1) antibody Fc-fragment, reduces IgG levels through neonatal Fc receptor blockade. Efgartigimod treatment has been investigated in generalized myasthenia gravis (gMG) via intravenous (IV) and subcutaneous (SC, coformulated with recombinant human hyaluronidase PH20) administration in ADAPT/ADAPT+ and ADAPT-SC/ADAPT-SC+ studies, respectively. Minimal symptom expression (MSE), defined as a Myasthenia Gravis Activities of Daily Living (MG-ADL) total score of 0 or 1, is explored as a novel proposed treatment target in gMG.

Methods: The proportion of acetylcholine receptor antibody positive (AChR-Ab+) participants in ADAPT+ (n=111) and ADAPT-SC+ (n=141) achieving MSE was assessed.

Results: In ADAPT, MSE was achieved in 44.6% of efgartigimod-treated participants vs 10.9% of placebo-treated participants at any time point up to 3 cycles. In ADAPT+, the number of participants achieving MSE at any time in up to 19 cycles was 40.5%. Eighty-one percent of efgartigimod-treated participants who achieved MSE in ADAPT also achieved MSE during ADAPT+; 23% who had not achieved MSE in ADAPT did so in ADAPT+. In ADAPT-SC, 45.5% and 41.3% of participants receiving efgartigimod PH20 SC or efgartigimod IV achieved MSE at any time in cycle 1, respectively. In ADAPT-SC+, the number of participants achieving MSE at any time in up to 9 cycles was 54.6%. Clinical improvements may not have been fully captured in OLEs (ADAPT+/ADAPT-SC+) due to the limited number of assessment timepoints.

Conclusion: Achievement of MSE was consistently seen across cycles in AChR-Ab+ participants of both ADAPT+ and ADAPT-SC+, similar to results demonstrated in ADAPT and ADAPT-SC.

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Fucoxanthin prevents Aβ-induced cognitive dysfunction *via* RAGE-dependent NF-κB signaling pathway

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Background: Alzheimer's disease (AD) is characterized by memory loss and cognitive dysfunction caused by neuronal cell death. The accumulation of β-amyloid (Aβ) is considered to be the major neurotoxin that triggers microglial activation, which drives the inflammatory cascade leading to synaptic dysfunction and apoptosis. Recently, the receptor for advanced glycation end-products (RAGE) has been identified as a novel mediator of nuclear factor-κB (NF-κB) pathway for neuroinflammatory response in AD. The present study investigated the neuroprotective effects of fucoxanthin, the most abundant marine carotenoid, against Aβ-induced microglial activation and cognitive impairment *via* inhibiting the RAGE/NF-κB signaling pathway in AD mouse model.

Methods: Passive avoidance test, Y-maze test, and Morris water maze test were used for behavioral test. Aβ accumulation, microglial activation, synaptic loss, RAGE and NF-κB regulated inflammatory proteins were determined by immunohistochemistry and western blotting.

Results: Oral administration of fucoxanthin (100 or 200 mg/kg) significantly improved Aβ-induced spatial learning and cognitive dysfunction *via* upregulating hippocampal post synaptic density protein (PSD-95). It showed a significant inhibitory effect on periplaque microglial activation by suppressing Aβ accumulation. Moreover, the compound suppressed NF-κB-mediated pro-inflammatory cytokines and their upstream enzymes by ameliorating RAGE, suggesting the inflammatory response is directly related to the RAGE/NF-κB signaling pathway.

Conclusions: Overall, the present results demonstrated that fucoxanthin ameliorated Aβ-induced microglia activation and cognitive dysfunction by targeting RAGE/NF-κB pathway-mediated inflammatory process. These findings provide a better understanding of the critical role of fucoxanthin in the prevention of AD and its potential as a promising candidate for anti-AD agents.

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Real-world reduction in oral corticosteroid utilization at 1-year following efgartigimod initiation

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Aim: To evaluate oral corticosteroid (OCS) usage at 1 year following efgartigimod (EFG) initiation.

Methods: Patients with generalized myasthenia gravis (gMG) using OCS pre-EFG initiation were identified from a United States medical and pharmacy claims database (based on information licensed from IQVIA: Longitudinal Access and Adjudication Data [LAAD] for the period April 2016−December 2023, reflecting estimates of real-world activity [all rights reserved]). Mean (standard deviation [SD]) average daily dose (ADD) of OCS was evaluated during the 3 months prior to, and at 6 and 12 months post-EFG initiation. To assess outcomes, de-identified Myasthenia Gravis Activities of Daily Living (MG-ADL) data collected in the "My VYVGART Path" patient support program were tokenized and integrated into the primary dataset.

Results: A total of 169 adults (aged ≥18 years) who were using chronic OCS pre-EFG initiation initiated EFG by December 31, 2022, and continued EFG for at least 12 months were included in the analysis. At 6 and 12 months post-EFG, respectively, 31 (18%) and 45 (27%) patients had no OCS usage. Overall mean (SD) OCS ADD was significantly reduced at 6 months (13.2 [13.9] mg/day, P0.001), and at 12 months (10.2 [12.1] mg/day, P0.001) post-EFG initiation compared with baseline (17.2 [13.7] mg/day). Among a subset of 72 patients (43%) who had both pre- and post-EFG MG-ADL scores available, best follow-up mean (SD) MG-ADL was significantly improved (from 8.3 [3.7] to 3.4 [2.8], P0.001).

Conclusion: The significant reduction of OCS usage observed at 6 months post-EFG initiation was retained at 12 months, while demonstrating MG-ADL response expected from EFG treatment.

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Optimizing Infliximab Dosing for Paradoxical Neurotuberculosis: A Case Report on Treatment Challenges and Decision-Making

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Introduction: Neurotuberculosis is a severe central nervous system infection. Paradoxical reactions can complicate its management, causing disease progression despite appropriate anti-TB treatment.This case report highlights the challenges in treating paradoxical reactions and the role of infliximab therapy.

Case Report: A 21-year-old HIV-negative female with disseminated tuberculosis (TB) and positive CSF(cerebro spinal fuild) TB PCR (polymerase chain reaction) was treated with a Category-1 regimen of anti-TB drugs.Initial imaging revealed right pleural effusion,multiple tuberculomas in the cerebellum and cerebral hemispheres, and meningeal thickening.Seven months into treatment,during the continuation phase she developed gradual right visual loss with temporal field deficit. MRI(magnestic resonance image) showed progression of suprasellar tuberculoma, with mass effect on the cavernous sinus, optic chiasm, pituitary stalk and hypothalamus. Despite normal pituitary function and negative CSF studies, her vision worsened. She was treated with high-dose IV (intravenous) Dexamethasone for 6-weeks, but vision deterioration continued. Subsequently, IV infliximab 6mg/kg was initiated at 0,2,6,12 weeks intervals along with anti-TB therapy for 18-months. Continuation phase included isoniazid, pyrazinamide and rifampicin.After 3-months of infliximab vision gradually improved with regression of tuberculoma.

Conclusion: This case underscores the challenges in managing paradoxical tuberculosis,especialy when the first-line treatment with high dose staeroids fail. Second-line treatments are thalidomide and infliximab, both TNF-alpha inhibitors, can be considered in such cases. In this case, infliximab was preferred due to the risk of thrombosis with thalidomide. The dose of infliximab was selected based on previous experience of inadequate response with lower doses.However, optimal dosing strategies and long term outcome require further investigations.

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How could diagnose MOGAD without MRI?

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Background: Establishing the role of HLA in diagnosis of MOGAD among patients with characteristic clinical manifestations, MOGAD IgG antibodies and contraindication for MRI.

Methods: We propose a case report of a 23 years old woman who presented with ocular pain succeeded by right monocular vision loss without recovery. One month later, she presented with progressive right hemiparesis. She have a history of idiopatic lumbar scoliosis which required surgical intervention with ZODIAC implant, being incompatible with MRI scan.

Results: According to hers symptoms, she performed a normal brain CT scan. In our clinic, we rule out MS, NMOSD and other diseases of the CNS based on clinical signs, brain CT and laboratory tests (infectious, immunologic, etc.). AQP4 IgG antibodies were negative, but IgG antibodies anti-MOG were present. In addition, the HLA testing were concludent for MOGAD (HLA-DRB1 *15:02:01). Based on MOGAD diagnostic criteria and despite the contraindication of performing an MRI scan, we still consider MOGAD diagnosis, due to clinical, immunological and genetic testing.

Conclusion: In particular cases, typing HLA profile could substitute MRI scan when it's not available or it's contraindicated. In conclusion, we need future studies on large cohorts of pacients to make a clear differential diagnosis between demyelinating disorders.

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Study of levels of oxidative stress and inflammation in rat brain tissue during Escherichia coli lipopolysaccharide-induced endotoxemia: modulatory effect of lycopene

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Introduction: Lipopolysaccharide (LPS) is an integral part of the cell walls of gram-negative bacteria, so during septic conditions, it leads to brain tissue damage. Lipopolysaccharide-induced endotoxemia produces excessive proinflammatory cytokines and reactive oxygen species in brain tissue. Lycopene (LYC) is a powerful antioxidant in the carotenoid plant pigments family (found in papaya, watermelon, grapefruit, apricot, and rosehip).

Aim: The objective of this research was to analyze the effect of lycopene in the prevention of brain damage caused by Escherichia coli lipopolysaccharide, by monitoring the level of oxidative stress (concentration of malondialdehyde-MDA, carbonyl groups-PCC, and reduced glutathione-GSH) and inflammation parameters (NF-kB, IL-6 and TNF-a), as well as the effects of lycopene supplementation on the investigated parameters.

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

Results: In the brains of rats treated with LPS, the concentrations of MDA, PCC, and GSH were significantly increased($p<0.01$), while the administration of LYC led to a decrease in the level of these parameters($p<0.01$). Administration of Lycopene in animals with endotoxemia(LPS+LYC group) significantly normalized the high levels of NF-kB, IL-6, and TNF-a in the brain tissue, compared to the LPS group($p<0.05$).

Conclusion: This study showed a significant therapeutic effect of lycopene, by exhibiting antioxidant and anti-inflammatory effects in brain tissue during endotoxemia. This work was supported by the project funded by the Ministry of Science of the Republic of Serbia(451-03-66/2024-03/200113).

Keywords: Lipopolysaccharide, Lycopene, Oxidative stress, Inflammation, Brain

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Guillain-Barré syndrome with five long-interval episodes and scoping review on recurrent Guillain-Barré syndrome

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Recurrent Guillain-Barré syndrome (RGBS) is a rare neurological condition occurring in approximately 2-6% of Guillain-Barré syndrome (GBS) patients. Due to its rarity, the clinical features and pathophysiology of RGBS remain to be elucidated. We present a unique case of RGBS with five recurrences at long intervals and scoping review of RGBS.
An eighty-one year old woman presented to our department with both leg weakness and paresthesia, the fourth relapse of GBS (mean interval between relapses 71 months) with stereotypical symptoms (distal leg weakness and paresthesia), IgM anti-GM1 antibody positivity and demyelinating neuropathy pattern. In addition, the patient recovered rapidly after intravenous immunoglobulin treatment in all attacks.
Our scoping review focused on RGBS such as our case using a specific criterion: clinically definite relapses with an interval of at least one year, objectively diagnosed GBS by nerve conduction studies or anti-ganglioside antibody assays, and three or more definite relapses. The analysis identified nine cases of GBS with 42 relapses since 1990 using the above criteria.
The results revealed a distinct subtype of RGBS with long intervals characterised by: 1) Stereotypical clinical manifestations across attacks 2) Positive presence of anti-ganglioside antibodies 3) Rapid response to intravenous immunoglobulin (IVIG) treatment.
This study suggests that anti-ganglioside antibodies or other immunological attacks play an important role in causing symptoms. This may be due to the existence of specific vulnerable sites in the peripheral nervous system that are susceptible to repeated antibody-mediated attacks. This comprehensive review provides insights into the complex immunological mechanisms of RGBS

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Viral polyneuropathy in an immunocompromised person: A case report

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Viral infections are associated with a wide range of nervous system complications. Upper and lower cranial nerve polyneuropathies have been reported from VZV infections. Chronic progressive polyneuropathies are observed in immunocompromised patients due to overlapping viral infections. A 76-year-old woman, with a past medical history of breast cancer three years ago followed by chemo and radiotherapy, was admitted to our hospital with complaints of dysphagia, dysphonia, left sided facial asymmetry, and progressive difficulty walking. Five months before she experienced a vesicular rash overlying the lumbar region and one week later left peripheral facial paralysis, difficulty swallowing, dysphonia and dysarthria. Two months before hospitalization, complained of febrile episodes with cough, followed by worsening of dysphagia and a progressive difficulty in controlling limbs. Neurological examination revealed hoarse voice, mild dysarthria, left sided peripheral facial asymmetry, decreased gag reflex, flaccid tetraparesis with inferior predominance, and hypoesthesia of the limbs. Laboratory findings: leukopenia and + anti-VZV. CSF indicated only elevated protein and pleocytosis. Brain+cervical MRI was unrevealing. Pulmonary scan showed bilateral viral pneumonia, not present before. Corticotherapy and Acyclovir were started. The electrophysiological study is suggestive for a demyelinating neuropathy with secondary axonal degeneration. We started IV immunoglobulin therapy. Unfortunately, her condition deteriorated leading to respiratory failure and subsequent death within a week of ICU admission. With our case, we emphasize the importance of recognizing and managing viral infections in immunocompromised patients as soon as possible. The rapid progression of her condition underscores the need for early recognition and intervention in similar clinical scenarios.

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Challenges in diagnosis and treatment of autoimmune encephalitis with anti-GAD antibodies – analysis of case series with clinical and MRI characteristics.

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Introduction: Autoimmune encephalitis with anti-glutamic acid decarboxylase antibodies (anti-GAD AE) is a rare but potentially life threatening condition. It is linked with many neurological syndromes such as stiff-person syndrome (SPS), cerebellar ataxia or limbic encephalitis. However, the clinical presentation may include several atypical features. The MRI analysis may show certain characteristic abnormalities but frequently has no diagnostic value.

Case Presentation: 1: A 59-year-old male admitted with tonic-clonic seizures. Initially treated with steroids later with intravenous immunoglobulin (IVIg) with good control of the symptoms.

2: A 23-year-old male with diplopia, impaired coordination and balance. Patient also presented mild cognitive impairment. The initial therapy was IVIg and azathioprine.

3: A 54-year-old male on admission presented clinical features typical for SPS. Following methylprednisolone treatment mofetil mycofenolate was administrated with significant clinical improvement.

In all cases laboratory tests confirmed the presence of anti-GAD antibodies in the serum. Only in the first patient, brain MRI revealed pathologies.

Conclusions: Our work shows variability of clinical and radiological presentation of anti-GAD AE. Our findings are only partially consistent with presentation described in the literature. None of the patients presented psychosis, but cognitive impairment and seizure occurred. We detected no malignancies, one patient had other autoimmune disorder. Interestingly, all of our patients were males, whilst the literature indicates the disease being more frequent among women. Brain MRI was moderately supportive for diagnosis. Immunosuppression mitigated symptoms in all cases. Our report can be of use for creating clear guidelines for anti-GAD AE diagnosis and management.

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Rituximab in AChR Positive Myasthenia Gravis Patients – A Highly Controversial Topic

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Before the introduction of new drugs since 2017, rituximab was one of the few therapeutic options available for patients with refractory generalized myasthenia gravis (gMG) who did not respond to conventional treatment. Rituximab is an anti-CD20 therapy that is used off-label for all neurological indications. Its effectiveness in MuSK-positive patients is well-established, but its efficacy in AChR-positive patients is less clear. There is a lack of consensus not only on its administration but also on the dosing regimen.

Our center administers this treatment in 33 cases (21 men and 12 women). The initial impetus was the clear neurological improvement observed in an MG patient who received rituximab for a hematological indication in 2009. Although rituximab is the drug of choice for patients with active MG, our patient cohort is relatively small, with all patients receiving at least two pulses. Among these, 23 achieved excellent results with minimal disease manifestation (relapse reduction $p \leq 0.0001$, QMGS decrease 10 IQR (3-10) $p \leq 0.0001$), and in 24 cases was possible to reduce chronic oral immunosuppressive therapy (especially corticosteroids 5 mg IQR (0-12.5), $p \leq 0.0001$), but also discontinuation of intravenous immunoglobulins. The greatest effect is seen in repeatedly hospitalized MG patients who cannot be stabilized despite repeated IVIG therapy and plasmapheresis. When initiating treatment, we are aware of the increased risk of infections, but so far, we have not observed significant adverse effects. This may be partly due to the rapid extension of the treatment interval between doses. In our cohort, the median interval between applications is 10 months (IQR 7-13.75) and the treatment duration is 4 years (IQR 1.5-10).

Rituximab is not intended for the treatment of all patients with active gMG. It is necessary to assess the risks of infectious complications and other comorbidities. Especially in patients with high disease activity and frequent exacerbations, this treatment is worth considering.

CONY

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Neuropathology

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Cognitive impairment and quality of life in sensorineural deafness

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Background and aims: Sensorineural hearing loss (SNHL) is a category of hearing loss (HL) that often leads to difficulty in understanding speech. HL is a serious condition that not only diminishes a patient's quality of life but can also lead to lifelong disability. The aim of study to assess the prevalence of cognitive dysfunction in acute and chronic sensorineural deafness. Methods. We studied 41 patients, mean age 48.05±16.9 year (19 women, 22 men), 20 of them with acute, 21 – with chronic SNHL as a result of acoustic trauma due to military action (in 19) and vascular injure (in 22). All patients had complete neurological and neuro-otological evaluation, including brain MRI, audiometry, air- and bone conduction, MoCA test and quality life assessment by MOS SF-36. We excluded subjects with total deafness, conductive deafness, previous history of neurological or psychiatric (stroke, tumor, dementia and other) compromise. Results. Average hearing levels of the audiograms did not differ significantly between the two groups. Neuro-otological symptoms included HL 30 dB, tinnitus (in 87.8%), vestibular symptoms (vertigo, dizziness, postural imbalance – in 31.7%). Average result of MoCA was 25.42±2.8 in acute and 23.13±3.32 chronic SNHL. Significantly difference observed in domains of attention and memory (p0.05). Decreased indicators of quality of life observed in both groups, but the decline in vital activity, social and emotional functioning was more significant in chronic SNHL (p0.05). Conclusion. SNHL are influence on cognitive dysfunction and quality of life which progressive with progressive hearing loss. More vulnerable is attention and memory.

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Carotenemi and neuropathy case report

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The 45-year-old female patient presents to the visit with numbness and a feeling of fatigue in the lower extremities.

Hardness and thickening of the soles of the hands and feet and their yellow color.
Laborator blood analysis shows high level of beta carotene.

The patient is the mother of a 23-year-old son, the soles of the hands and feet with corotenemia.

In the objective neurological examination, a decrease in patellar and achilles osteo-tendinous reflexes is observed. Superficial sensitivity reduced in the form of short socks.

Electroneurography of the inferior sides: Electroneurographic data of the examined nerves suggest axonal sensorimotor polyneuropathy of a metabolic etiology.

Carotenemia is a condition in which yellow or orange colored skin due to high levels of beta-carotene in the blood.

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Parkinson's Disease

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Real life Experience with Foslevodopa/Foscarbidopa in an Outpatient Clinic

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Background: Foslevodopa/foscarbidopa is a continuous subcutaneous infusion aimed to improve motor fluctuation in patients with advanced levodopa-responsive Parkinson's disease (PD). We report our experience with this novel medication.

Methods: Eight PD patient, 4 males, with a mean age of 66 years (range 45-76 years) with a mean disease duration of 15 years (range 8-25 years) and a mean levodopa equivalent dose of 875.5 mg (range 187.5-1614) were converted to a mean of 2,064 mg (range 752-3072 mg) foslevodopa/foscarbidopa 24 hour subcutaneous pump. Change in patient global clinical impression (CGI) of physicians and patients was documented as well as adverse events.

Results: In our cohort, at 1 month follow-up, physician's CGI and patients' CGI improved in all patients. Adverse events included skin reactions: erythema (n=6), abscess (n=2), psychosis (n=1), nausea and vomiting (n=1) and night-time dyskinesia (n=1). All adverse events were transient and did not require discontinuation of the medication.

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Measurement of cross-sectional area of vagus nerve as an imaging biomarker in patient`s with early Parkinson's disease

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Background: Several studies have reported atrophy of the vagus nerve (VN) in PD, but mostly been conducted on advanced patients. This study aimed to compare VN size in PD patients according to the disease stages and non-degenerative parkinsonism (non-dPD) patients using high-resolution ultrasonography (HRUS).

Method: We evaluated patients presenting with parkinsonism. Experienced neurologist who blinded to clinical information conducted HRUS examinations to measure the cross-sectional area (CSA) of the VN at the level of carotid artery bifurcation.

Results: Total 57 consecutive patients (44 with PD and 13 with non-dPD (scans without evidence of dopaminergic deficits))enrolled. Among PD group, 36 were in early-stage [Hoehn &Yahr stage (HY) ≤ 2.5], and 8 were in advanced-stage (HY ≥ 3). The mean CSAs of right VN were significantly smaller in the PD compared to non-PD (PD 1.73 mm2 vs. non-PD 2.00 mm2, P = 0.049). Right VN atrophy was more distinct in advanced-stage PD group than in the early-stage PD group (late PD 1.54 mm2 vs. early PD 1.77 mm2, P = 0.035). The CSA of the left VN tended to be smaller in the PD group and advanced-stage PD group compared to the non-PD group and early-stage PD group, respectively (late PD 1.31 mm2, early PD 1.35 mm2, and non-PD 1.47 mm2).

Conclusion: This study suggests that the VN size measured by HRUS could be a useful supplementary method indicating PD. VN size in PD might be a disease-specific marker rather than progression marker. Additional validation studies on large samples are further needed.

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Impact of IPX203 (CREXONT®) on Parkinson's patients' motor states upon awakening: analysis of patient diary data

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Objective: To evaluate "On" upon awakening in Parkinson's disease patients taking IPX203 in the RISE-PD phase 3 clinical trial.

Background: IPX203 is a novel extended-release, oral carbidopa-levodopa (CD-LD) formulation that provides fast onset and prolonged duration of "On".In RISE-PD, IPX203 demonstrated significant increase vs immediate-release (IR) CD-LD in "Good On" time per day and "Good On" time per dose.

Methods: We performed an analysis of Hauser diary data from the 495 subjects that completed the RISE-PD study.Outcome measures evaluated over the three days prior to study visit:the percentage of times waking up "On" ("On" upon awakening), the percentage of patients that never recorded "Off" upon awakening, and the percentage of patients that never recorded "On" upon awakening.

Results: At study entry, patients reported waking up "On" 17% of the time.At end-of-study (EOS), "On" upon awakening was 40% in patients on IPX203 vs 27% in patients on IR CD-LD (p=0.0004).At study entry, 8% of patients never recorded "Off" upon awakening.At EOS, 26% of patients on IPX203 never recorded "Off" upon awakening vs 17% in the IR CD-LD group (p=0.0224).The percentage of patients that never recorded "On" upon awakening decreased from 73% to 47% with IPX203 vs 71% to 59% for IR CD-LD (p=0.0067).

Conclusion: IPX203 treatment resulted in significant increase in patients waking up "On" during the study period.At EOS, a significantly higher percentage of patients on IPX203 were never "Off" upon awakening vs patients on IR CD-LD.Significantly lower percentage of patients recorded to never be "On" upon awakening in the IPX203 group vs IR CD-LD.

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Access to and use of device-aided therapies in Parkinson`s disease in France from 2015 to 2021: the PARK-DAT study

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Objective: The aim of the PARK-DAT study was to measure access to and use of device-aided therapies (DAT) for Parkinson`s disease (PD) in France from 2015–2022.

Background: DAT, which include deep brain stimulation (DBS), levodopa-carbidopa intestinal gel (LCIG) infusion and continuous subcutaneous apomorphine infusion (CSAI) are effective treatment options for advanced PD patients. Disparities in access have been highlighted in several countries.

Methods: Data were collected retrospectively from the French administrative health care database (Système National des Données de Santé [SNDS]). The incidence of DAT initiation in PD patients was calculated for each year of the study period. Incidences were also calculated by year and by region. Incidence rates were standardized by age group (every 10 years) and sex.

Results: 8,829 patients (mean age 68,7±10,3 years; 43.4% women) were initiated on a DAT between 2015 and 2021 (+41.8%). Of these, 6,873 received CSAI (+58.9%), 1,592 DBS (-20.7%) and 364 LCIG (+152.9%). Prescribers were predominantly hospital centers (74.6%). A small proportion of DAT switches and combinations were observed. Regional mapping of standardized annual incidence of DAT initiation in PD patients suggests disparities in access.

Conclusions: In some countries the most widely used DAT is DBS (Poland, Norway, Germany) or LCIG (Denmark), however the DAT most frequently used in France between 2015 and 2021 was CSAI, while the use of DBS declined. The specific features of the French healthcare system (reimbursement rates, availability of homecare nurses) may explain this distribution and the high prevalence of PD patients treated with a DAT.

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Novel objective tool to assess tremor reveals unilateral focused ultrasound improves tremor bilaterally

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Background: Tremor in Essential tremor (ET) and tremor dominant Parkinson's disease (TDPD) is assessed by subjective observations in patients undergoing focused ultrasound thalamotomy (FUS), a minimally invasive procedure intended to alleviate tremor in these patients.

Objective: To develop an objective tool for tremor assessment. First, we showed that the proposed tool reproduces known clinical dynamics on the treated hand, then we used it to evaluate the non-treated hand.
Methods: Using image and signal processing that utilized images of Archimedes spiral drawings, we created a tool to analyze tremor. We showed that the proposed tool reproduces known clinical dynamics on the treated hand. We then used it to evaluate the clinical dynamics on the non-treated hand.

Results: Using our tool, we demonstrated a significant reduction in tremor following FUS thalamotomy among 132 ET patients and 26 TDPD in the treated hand using the drawings of Archimedes spirals up to 1 year following the procedure. Thus, we reproduced known clinical data and therefore validated the proposed tool. We then were able to demonstrate a significant improvement in the non-treated hand as well as a significant deterioration in the efficacy of FUS over time.

Conclusions: Our objective method, which incorporated image processing and signal processing, provided a quantitative measure of tremor reduction following FUS thalamotomy. It demonstrated significant improvement in tremors in the treated and non-treated hands following FUS thalamotomy, as well as deterioration in the efficacy of treatment over time. If replicated in other studies this method may complement current subjective assessments.

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Novel objective tool to assess tremor reveals unilateral focused ultrasound improves tremor bilaterally

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Conclusions: Our objective method, which incorporated image processing and signal processing, provided a quantitative measure of tremor reduction following FUS thalamotomy. It demonstrated significant improvement in tremors in the treated and non-treated hands following FUS thalamotomy, as well as deterioration in the efficacy of treatment over time. If replicated in other studies this method may complement current subjective assessments.

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Ten-year outcome of Focused Ultrasound Thalamotomy in Tremor Dominant Parkinson Disease

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Background: MRI guided focused ultrasound (FUS) thalamotomy is effective in tremor relief in tremor dominant Parkinson's disease (TDPD) patients. Long-term reports are sparse with the longest follow-up reported to date being 5 years. Thus, weather efficacy remains beyond 5 years is unknown.

Methods: We report on the efficacy of FUS VIM-thalamotomy for tremor relief in a patient with TDPD 10 years following the procedure. A 66-year-old right-handed male suffering for 7 years from TDPD suffered from severe action tremor refractory to medication and limited to his right hand. Due to severity of tremor, he required assistance in activities of daily living. Additional PD symptoms including rigidity and bradykinesia were well controlled with Stalevo®. Severity of disease was measured with Unified Parkinson`s Disease Rating Scale (UPDRS) part III.

Results: Clinical Rating Scale for Tremor (CRST) score was 44 in the right hand and 0 on the left. UPDRS part III score was 22. The patient underwent FUS VIM thalamotomy. Immediately following treatment, the patient was tremor free. He was immediately able to perform activities of daily living. He reported no adverse effects. At 5 years follow-up his CRST score was 0 in the treated hand and 2 in the left hand and the UPDRS was 1. At ten years his CRST score is 4 in the right hand and 11 in the left hand, UPDRS is 16.

Conclusion: We conclude that in our TDPD patient unilateral FUS VIM-thalamotomy was effective and safe and provided tremor relief for 10 years.

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Multimodal forms of art therapy as a complementary treatment for Parkinson's disease

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Objectives: Assessing the impact of art therapy on treatment outcomes and quality of life in Parkinson`s disease.

Background: In addition to medical treatment, art therapy plays an extremely important role in Parkinson`s disease. Various procedures and methods are used to stimulate compensatory and redundancy mechanisms and neuroplasticity. Based on the results of numerous scientific researches, as well as empirically, the extremely positive effect of various forms of art on the treatment of Parkinson`s disease has been confirmed, either by accepting (observing, listening to...) art, or through personal artistic-creative expression.

Methods: The study was conducted on two groups of 30 patients with Parkinson`s disease. One group, in addition to drug therapy, goes through cycles of art therapy (art and graphic expression and music therapy) for three years, while the control group remains exclusively on drug therapy. Uric acid levels were determined for all patients at the beginning of the study and will be monitored during and at the end of the study. All participants will be continuously evaluated by completing validated questionnaires and scales.

Results: Data collection is still in progress. After the first cycle of workshops, we noticed improvement in several domains, including motor skills, cognition and emotional awareness.

Conclusion: The first results show a positive effect of art therapy on the subjects, but it is necessary to conduct more cycles of workshops in order to confirm their effectiveness.

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Time-dependent progression of α-synuclein pathology from the olfactory bulb to other brain regions after intranasal rotenone administration in mice

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Our study takes a unique approach to understanding Parkinson's disease (PD). We focus on the time-dependent progression of α-synuclein (α-syn) pathology, a key feature of PD, from the olfactory bulb (OB) to other brain regions. This progression is studied after intranasal rotenone microemulsion administration in mice for 9 weeks. Our study is distinct in that we were unable to track the progression of α-syn pathology from OB to striatum in previous research. In the present study, we evaluated the time-dependent progression of PD-like pathology by giving rotenone intranasally for 5.5 months in C57Bl/6 mice. We performed olfactory and motor impairment tests and examined the expression of markers of α-syn accumulation, glial cell activation and dopaminergic neurodegeneration after 3, 4 and 5.5 months of rotenone exposure by western blotting and immunofluorescence techniques. Depending on the surrounding environment, astrocytes play either a protective (A2)/proinflammatory role (A1), so we explored the role of A1 and A2 astrocytes in modulating PD-like pathology. We observed a time-dependent progression of α-syn accumulation from OB to other brain regions, including the mid-brain and cortex. Analogously, there was a time-dependent behavioural impairment, OB atrophy, spreading of α-syn pathology, neuroinflammation and neurodegeneration. Our findings also established a link between astrocyte activation and dopaminergic (DAergic) activity. This chronic progressive mouse model of PD mimics the progression of PD-like pathology in PD patients. Thus, it is suitable for identifying the disease biomarkers and testing potential disease-modifying interventions for PD.

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Hyposmia in Parkinson`s Disease: Demographic and Cognitive Associations

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As known, hyposmia is one of the most common, prodromal nonmotor feature of Parkinson`s disease. This Study investigates the relationship between hyposmia, and Cognitive status of patients with Parkinson's disease.

Methods: Data from 54 Parkinson`s disease patients were analyzed, focusing on 20 individuals reporting impaired olfactory function. Patients with health conditions like nasal polyps, allergies and cold as well as hormonal imbalances were excluded from the study. Demographic and cognitive parameters, including patient age, sex, and cognition by Mini-Mental State Examination (MMSE) scores were investigated. Statistical comparisons and correlation analyses conducted using the SPSS - 21 (IBM SPSS Statistics, Armonk, NY].

Results: Patients with hyposmia had a mean age of 64.8 (4.4 SD) years, significantly higher than the mean age of 58.2 (3.2SD) years in patients without hyposmia (p 0.05). MMSE scores were lower in the hyposmic group (mean: 21.1(2.2 SD) compared to non-hyposmic patients (mean: 26.6 (1.4SD), p 0.05). A significant negative correlation (r = -0.47) was observed between age and MMSE scores in the hyposmic cohort. Males comprised 55.0% of the hyposmic group.

Conclusion: According to the above research in Parkinson`s disease patients, hyposmia correlates with older age and lower MMSE score, emphesizing its potential role as an indicator of expected cognitive dysfunction. Further investigations in this direction are required.

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Profile of motor and non-motor symptoms in patients with Parkinson`s disease indicated for treatment with intestinal pump systems

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Introduction: Treatment with intestinal pump systems in patients with Parkinson`s disease (PD) is currently available via levodopa-carbidopa intestinal gel (LCIG) or levodopa-entacapone-carbidopa intestinal gel (LECIG). The choice of the appropriate treatment depends on the experiences and preferences of the referring centre and physician.

Methods: The total number of 30 subjects with advanced PD were included in the study. All subjects were indicated for treatment with particular intestinal pump system. Before initiation of treatment all subjects underwent cognitive testing (MoCA), an assessment of PD symptoms according to MDS-UPDRS, motor fluctuations (UdysRS), non-motor symptoms (MDS-NMS), autonomic symptoms (SCOPA-AUT), wearing-off phenomenon (WOQ-9), gastrointestinal symptoms (GIDPS-PD), impulsivity (QUIP-RS) and quality of life (PDQ-8).

Results: The cohort consisted of 15 patients indicated for LCIG treatment (3 women; mean age 73.66±5.78 years) and 15 patients indicated for LECIG treatment (6 women; mean age 67.53±6.99 years). Both groups had similar cognitive status according to MoCA (median LCIG 21 vs. LECIG 23; p=0.259). Patients indicated for LCIG were found to have significantly more severe non-motor symptoms in the MDS-NMS (P=0.009) and its subscales - depression (p=0.002), anxiety (p=0.046), cognition (p=0.22), digestion (p=0.049) and in the PDQ-8 scale (p=0.020). There were no significant differences in other parameters.

Conclusion: We confirmed that non-motor symptoms are different in patients referred for treatment with LCIG and LECIG. Patients with less severe neuropsychiatric symptoms were preferred for treatment including catechol-O-methyltransferase (COMT) inhibitor. No significant differences were found in cognitive status, motor symptoms and demographic parameters.

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Pain in Parkinson`s disease: clinical and laboratory markers

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Introduction: Sensory nerve degeneration and nociceptive hypersensitivity involving α-synuclein play a role in the pathogenesis of pain in Parkinson`s disease (PD).

Aim: To assess pain and its relationship with the concentration of α-synuclein in blood plasma in patients with PD.

Methods: 64 patients with PD who were undergoing examination and treatment at the Center for Patients with PD were examined. Patients were divided into 2 groups: 1 gr. (38 people) - akinetic-rigid, 2 gr. (26 people) - mixed form. Control - 30 people without signs of neurodegenerative disease. To assess pain, a visual analog scale and the McGill questionnaire were used. Quantitative determination of alpha-α-synuclein in blood plasma was performed by the sandwich method of immunoenzyme analysis using the SEB222Hu kit.

Results: No significant gender and age differences were found between the groups (p=0.719 for gender and p=0.167 for age), no difference was found on the UPDRS scale (p=0.856). Types of pain in PD: musculoskeletal, radicular, pain associated with fluctuations. Its intensity correlated with the duration of the disease and dominated in the akinetic-rigid form. Patients with PD have higher α-synuclein concentration compared to controls.

Conclusions: Pain syndrome in PD correlates with the severity of the disease and prevails in the akinetic-rigid form. The level of α-synuclein does not differ in different forms of PD. The concentration of α-synuclein in fasting plasma can be considered as a biomarker of the severity of pain in patients with PD.

Keywords: Parkinson`s disease, pain, markers, synuclein.

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Rehabilitation

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Ways of Enhancement of the Efficacy of Transcranial Direct Electrical Stimulation in the Elimination of Post-Stroke Disorders

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Introduction: Transcranial direct current stimulation (tDCS) is a non-invasive form of neuromodulation that has shown potential in the elimination of motor, cognitive, speech and other post-stroke disorders.

The aim of this review was to analyze the evidence on the effectiveness of tDCS and the possibility of enhancing its effectiveness in restoring impaired functions in patients after stroke.

Methods: Search of literature was conducted in the PubMed, Google Scholar and Scopus databases according to the following criteria: 1. The effectiveness of tDCS in the elimination of neurological disorders after stroke; 2. Ways to enhance the neuroprotective effect of tDCS in rehabilitation of post-stroke patients.

Main results: A meta-analysis on the first question showed that cathodal tDCS exerts a neuroprotective effect by reducing infarct size and improving neurological deficits after focal ischemic stroke.

Cerebrolysin is currently approved as a neuroprotective medicine for the treatment of ischemic and hemorrhagic stroke. It exhibits neurotrophic effects, promotes neuronal sprouting, improves cell survival, and stimulates neurogenesis. The combination of Cerebrolysin and standard rehabilitation therapy demonstrated additional benefit in motor function recovery and corticospinal tract plasticity among patients with severe motor impairment.

Based on these data, we chose the combined use of tDCS and Cerebrolysin as a way to improve the effectiveness of rehabilitation in post-stroke patients.

Conclusion: Future clinical studies are needed to evaluate the efficacy of tDCS and Cerebrolysin in combination in patients with chronic stroke in order to develop an optimal method for their combined use. For this purpose, the CİNEMA-Cerebrolysin Neuro Modulation Azerbaijan study is currently underway in Azerbaijan.

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"Tele-CO-OP: A Feasible and Effective Telerehabilitation Approach for Enhancing Participation in Chronic Acquired Brain Injury Survivors"

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Background: Acquired brain injury (ABI), including stroke and traumatic brain injury (TBI), results in long-term participation restrictions, highlighting the need for accessible telerehabilitation services to support community integration.

Objectives: This research explored multidimensional participation in adults with chronic ABI and developed a telerehabilitation protocol, tele-CO-OP, based on the Cognitive Orientation to Daily Occupational Performance approach, to enhance participation.

Phase 1:
Methods: Twenty-five adults (≥6 months post-ABI) were assessed using the Canadian Occupational Performance Measure (COPM; subjective participation) and the Mayo-Portland Adaptability Inventory (MPAI-4; objective participation).

Results: Participants reported challenges in subjective and objective participation, with profiles varying by disability level except in social and leisure areas. Partial compatibility was noted between subjective importance and objective limitations.

Phase 2:
Methods: A pilot randomized controlled trial (RCT) with 16 participants evaluated tele-CO-OP`s efficacy. Assessments were conducted at baseline, post-intervention, and three-month follow-up. Outcomes included subjective (COPM, PQRS) and objective (MPAI-4) participation, executive function, self-efficacy, and caregiver burden.

Results: Pooled data revealed significant improvements in participation outcomes, with medium to large effect sizes. Frequency of leaving the house increased, and trends in self-efficacy were noted. Improvements were partially maintained at follow-up. Participants reported high satisfaction and retention rates.

Conclusion: Tele-CO-OP demonstrates feasibility and preliminary efficacy in improving participation for adults with chronic ABI. Larger controlled studies are recommended to confirm its effectiveness.

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Sleep

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The Role of Polysomnography and Multiple Sleep Latency Testing: A Case of Narcolepsy Misdiagnosed as Epilepsy

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Background: Narcolepsy is a chronic sleep disorder characterized by excessive daytime sleepiness, sleep paralysis, and disrupted nocturnal sleep. This condition can present diagnostic challenges, especially when symptoms overlap with other neurological disorders. We report a case of central hypersomnia in a patient previously misdiagnosed with epilepsy, emphasizing the importance of comprehensive sleep studies such as polysomnography (PSG) and multiple sleep latency testing (MSLT), for accurate diagnosis.

Case Presentation: A 32-year-old female presented with a 13-year history of recurrent episodes of altered consciousness, extreme drowsiness, slurred speech, and prolonged post-episode sleep. Symptoms often occurred during activity, with preserved automatic movements. The patient reported vivid dreams, sleep paralysis, and hypnagogic hallucinations. Initially misdiagnosed with absence epilepsy, she was treated with anticonvulsants without clinical improvement.

Diagnostic evaluations included: MRI: Revealed an incidental arachnoid cyst in the parietal lobe.
Video-EEG Monitoring: Identified 3 episodes of drowsiness with sleep onset (20–40 seconds), hypnagogic jerks, and disrupted sleep architecture, with all cycles initiating in REM sleep. PSG and MSLT: Showed fragmented nocturnal sleep and 4 sleep-onset REM periods (SOREMPs) during daytime naps, confirming narcolepsy diagnosis.

Conclusion: This case underscores the diagnostic challenges of narcolepsy when symptoms mimic epilepsy. PSG and MSLT provided definitive evidence, demonstrating fragmented nighttime sleep, shortened sleep latency, and multiple SOREMPs. Early recognition and accurate diagnosis can significantly improve patient outcomes by guiding appropriate therapeutic strategies.

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Prevalence of Sleep Disorders in Adults with Attention Deficit Hyperactivity Disorder (ADHD) attending specialist clinic in Northwest Ireland

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Background: Sleep disorders are common in ADHD, however, in contrast to children, only few studies have been conducted in adult populations.

Objectives: a) To determine what proportion of adults with ADHD suffer from sleep disorders, b) To identify the sleep disorders that co-occurring most commonly with ADHD c) To examine the relationship between ADHD subtype and sleep disorders

Method: Consecutive patients with ADHD. Scales administered: Pittsburgh Sleep Quality Index (PSQI) to assess sleep quality and Sleep Disorders Symptoms Checklist 17 which screens for 6 sleep disorders: insomnia, obstructive sleep apnoea (OSA), restless legs syndrome (RLS), circadian rhythm, narcolepsy, and parasomnias.

Results: 132 diagnosed with ADHD, mean age 30.26 (SD:10.17), 75(56.8%) females. Eighty-four (63.6%) had combined type, 47 (35.6%) inattentive and 1 (0.8%) hyperactive. Reduced sleep quality (PSQI 5 and above) had 121 (91.7%). Twenty-eight (21.2%) were screened negative for any sleep disorder, 37 (28%) screened positive for one sleep disorder, and the rest 70 for two or more. The most common sleep disorder was insomnia (n=77, 58.3%) followed by OSA (n=58, 43.9%) and RLS (n=48, 65.4%). The majority (n=74, 75.5%) were evening circadian type. Those with combined subtype were significantly more likely to found with RLS (x2= 12.154, p0.001, and parasomnias (x2= 5.685, p=.017) compared to inattentive subtype.

Conclusions: Hight prevalence of sleep disorders in adult ADHD. They are more likely to display an evening circadian type which may be linked to alterations in melatonin levels. Those with combined type were more likely to have RLS and parasomnias.

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Stroke

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Splenium of Corpus Callosum Infarction in a 60-Year Old Male- A Case Report

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Introduction: Corpus callosum infarction, while relatively rare, is a clinically significant neurological event, characterised by diverse and subtle manifestations.

Case report: This case report discusses a 60-years old male patient with a medical history of hypertension, coronary artery bypass grafting (CABG) and diabetes mellitus, who presented with cognitive changes and gait abnormalities initially misattributed to metabolic causes. Imaging studies revealed a hypodense area in the left corpus callosum on CT, suggesting and ischemic event. Magnetic resonance angiography (MRA) indicated hyperintensity in the left corpus callosum on T2 weighted images, with associated damage to the periventricular centrum semiovale, and multiple ipsilateral lacunar infarcts. Notably the bilateral internal carotid arteries (ICA) showed symmetric trajectories but a kinking of a right petrous tract, alongside approximately 70% stenosis over a 2cm segment of the left petrous tract. The patient also presented with a dominant right vertebral artery, and both the basilar artery and posterior cerebral artery (PCA) appeared normal, though a fetal aspect of the right PCA was noted. The patient was managed conservatively with dual antiplatelet therapy (DAPT) and 80mg of atorvastatin. Remarkably, significant functional recovery was observed, leading to a satisfactory quality of life post treatment.

Conclusion: This case emphasizes the importance of recognizing corpus callosum infarction as a crucial neurological event. Timely diagnosis and appropriate management strategies can greatly enhance patient outcomes, warranting further investigations into the condition`s implications and treatment options.

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Diffusion-weighted MRI in Anterior Spinal Artery Stroke of the Thoracic Spinal Cord presenting with Incomplete Brown-Séquard Syndrome

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Background: Spinal cord infarction is unusual, accounting for 1% of all cases of stroke in general hospital. Brown-Séquard Syndrome classically results from spinal cord hemisection, most commonly due to trauma and occasionally from tumor or infarction. Most patients experience an incomplete Brown-Séquard Syndrome with only partial sensory and motor impairment. The diagnosis of spinal cord infarction is primarily made on clinical grounds and neurological examination. Definitive diagnosis of spinal cord infarction in the acute stage is not always possible even with conventional MRI. Thus, application of the diffusion-weighted imaging(DWI) technique to the spinal cord has been expected to allow technique to the spinal cord infarction and more precise evaluation of the status of the disease. Case; A 68-years-old hypertensive man presented an incomplete Brown-Séquard syndrome of sudden onset. Neurological examination revealed weakness of right side lower extremity, and decrease of pinprick and temperature sensation below the T1 dermatome on the left side. The proprioception was intact bilaterally. Thoracic MRI exhibited intramedullary hyperintensity on the ventral two third and right lateral portion of the cord at T1 vertebral level on T2WI and DWI. The mean ADC value of the lesion on the DWI decreased compared with the mean ADC values of the adjacent normal spinal cord.

Conclusion: We report an example of the usefulness of DWI for diagnosing patients with suspected spinal cord infarction, and a rare case of anterior spinal artery stroke of the thoracic spinal cord presenting with incomplete Brown-Séquard Syndrome.

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Cases of Ischemic Stroke with Rare Mechanism Diagnosed through Histopathology of Thrombus Obtained through Thrombectomy.

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Background and aims: Pathological examination of the thrombus obtained through endovascular thrombectomy could provide clues to the mechanism of stroke. However, the stroke mechanism cannot be directly identified based on the pathological results.

Methods: We report two rare cases in which pathological examination of the thrombus directly contributed to the diagnosis of stroke mechanism.

Results: Case1. A 60-year-old woman presented to the emergency department with right hemiparesis. Left ICA occlusion was diagnosed, and several attempts of endovascular thrombectomy were performed, and a white, semitransparent substance was extracted. The specimen was sent to the pathology laboratory, where tumor cells containing myoid stroma were found. Echocardiography revealed a 5x3cm heterogenous echogenic mass in the left atrium. The patient was referred to cardiac surgery, and the resected tumor was ultimately diagnosed as a cardiac myxoma. Case2. An 81-year-old man who was being treated for pneumonia developed altered mental status. CT angiography revealed basilar artery occlusion, and emergency endovascular thrombectomy was performed. Pink and yellow materials were extracted. Pathological examination of the thrombus revealed a fibrinous exudate containing inflammatory cells, leading to the suspicion of infective endocarditis-related stroke. Subsequent echocardiography were performed, and a 1cm-sized mobile echogenic mass, which was not observed in the previous echocardiography 3 weeks ago, was observed in the mitral valve.

Conclusions: Understanding the characteristics of thrombus could be helpful in the differential diagnosis of rare causes of acute ischemic stroke.

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Simultaneous Multifocal Intracranial Hemorrhages from Ruptured Mycotic Aneurysms – A Case Report

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Intracranial mycotic aneurysms (IMAs) are rare neurovascular lesions that usually involve the smaller distal middle cerebral artery cortical branches, with only about 5% of the cases occurring in the posterior cerebral artery. Spontaneous rupture resulting in intracerebral and subarachnoid haemorrhages is an unusual and catastrophic event which results to poor neurological outcome and high mortality rate. In this paper, we report the case of a 17-year-old, hypertensive, male with multifocal ruptured aneurysms involving the left P2P segment of the LPCA and cortical M4 segment of the RMCA, with subsequent resection of the former. Anti-streptolysin O titer was elevated and transthoracic echocardiogram revealed poor coaptation of aortic valve leaflets with no evidence of vegetation. Histopathology revealed diffuse inflammation, reactive fibroblasts, thrombus and disrupted wall, with no microorganism isolated. Currently, the clinical diagnosis of IMA is based on documentation of aneurysm by angiography in the presence of predisposing infection, which is found to be incomplete, general, and non-discriminatory. Hence, Kannoth, et.al, proposed a scoring system based on the presence of specific clinical and radiographic characteristics, where patient was categorized as clinically definite IMA.

Identification of angiographic features of mycotic aneurysm in cerebral imaging is essential in arriving at proper and early diagnosis, resulting in better patient outcomes. Angiographic features which set IMA from other types of aneurysms include peripheral position, uneven outline, fusiform shape, multiplicity, and poorly defined neck. Currently, this is the first case reported in the Philippines involving intracranial mycotic aneurysms of both anterior and posterior vasculatures with subsequent rupture.

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Tailored Cognitive Rehabilitation For Post Stroke Reading Deficits

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Background: Post-stroke reading deficits, commonly referred to as alexia, significantly impact a patient`s quality of life and cognitive function. Tailored cognitive rehabilitation strategies aim to address these specific deficits by customizing interventions to meet individual needs. Understanding the effectiveness of such targeted approaches can lead to improved outcomes for stroke survivors experiencing reading difficulties.

Aims and Objectives: To develop and implement tailored cognitive rehabilitation programs designed specifically for patients with post-stroke reading deficits. (2) To assess the effectiveness of personalized interventions in enhancing reading abilities and overall cognitive function.(3) To identify the underlying cognitive processes involved in reading and how they are affected by stroke.

Methods: A cohort of stroke patients with identified reading deficits underwent comprehensive assessments to determine their specific challenges. Tailored rehabilitation programs were designed, incorporating various techniques such as phonological training, visual scanning exercises, and contextual reading strategies. Progress will be measured using standardized reading assessments over multiple sessions.

Results: A total of 70 participants with post-stroke reading deficits were identified. Of these 20 had persistent deficits and 5 went through intensive tailored rehabilitation. All patients showed improvement in reading and language function at 3 months follow up. Discussion This study contributes to the understanding of Tailored cognitive rehabilitation for post-stroke reading deficits involving structured reading exercises and functional reading tasks to reinforce neural pathways and boost confidence, ultimately enhancing the patient’s overall quality of life.

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Association of body composition indices with cardiovascular outcomes: a nationwide cohort study

Tae-Jin Song

Objectives: We aimed to investigate the association between body composition and cardiovascular outcomes according to BMI categories in the Korean general population.

Methods: A total of 2,604,401 participants were enrolled in this nationwide cohort study using the National Health Insurance Service-Health Checkup data set. Predicted lean BMI (pLBMI), body fat mass index (pBFMI), and appendicular skeletal muscle mass index (pASMMI) were calculated using validated anthropometric prediction equations. A multivariable time-dependent Cox regression analysis was conducted to assess the association with cardiovascular outcomes. The results were presented with adjusted hazard ratios (HRs) with 95% confidence intervals (CIs), considering BMI categories (BMI 18.5, BMI 18.5-24.9, BMI 25-29.9, and BMI ≥ 30).

Results: Higher pLBMI and pASMMI were correlated with a reduced risk of composite cardiovascular outcomes. For pLBMI, HR was 0.910 (95% CI: 0.908, 0.913, P 0.001) for males and 0.905 (95% CI: 0.899, 0.910, P 0.001) for females. For pASMMI, HR was 0.825 (95% CI: 0.820, 0.829, P0.001) for males and 0.788 (95% CI: 0.777, 0.800, P0.001) for females. Conversely, a higher pBFMI was associated with an increased risk, with HR of 1.082 (95% CI: 1.071, 1.093, P0.001) for males and 1.181 (95% CI: 1.170, 1.192, P0.001) for females. Subgroup analysis based on BMI categories revealed no significant risk association for pBFMI in the BMI

Conclusions: Our results highlight the value of pLBMI, pBFMI, and pASMMI as variables for assessing risk of composite cardiovascular outcomes. The significance of indicators may vary depending on BMI categories.

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Vasculitic Stroke in Polyarteritis Nodosa – A Case Report

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Polyarteritis nodosa (PAN) is a rare autoimmune vasculitis characterized by systemic inflammation of medium-sized arteries, leading to diverse clinical manifestations. We present a challenging case of a vasculitic stroke in a patient diagnosed with PAN. A 57-year-old male with a history of PAN presented with sudden-onset no verbal output and right sided weakness. Neuroimaging revealed an acute ischemic stroke involving left frontal lobe, the corona radiata and left insula. Laboratory investigations, including serological markers, supported the diagnosis of active PAN with central nervous system involvement. The patient was promptly initiated on high-dose corticosteroids, leading to a gradual improvement in neurological deficits over several days.

This case underscores the importance of considering vasculitis, particularly PAN, in the differential diagnosis of strokes, especially when multiple vascular territories are affected. Timely recognition and aggressive immunosuppressive treatment are crucial in managing vasculitic strokes associated with PAN, aiming to prevent further neurological complications and enhance overall patient outcomes. This report contributes to the expanding knowledge on the diverse neurological manifestations of PAN, emphasizing the need for multidisciplinary collaboration between rheumatologists and neurologists for accurate diagnosis and optimal management of this complex condition.

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Post-stroke Care Planning: Bridging Shared Concerns and Diverging Needs of Stroke Survivors and Caregivers

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Background & Objectives: Ischemic stroke has lasting impacts on both stroke survivors and their families. To support their adaptation better, tailored care plans are needed to address the needs of both patients and caregivers. This study aimed to evaluate the shared and different needs of ischemic stroke patients and their caregivers.

Method: A cross-sectional, qualitative survey was conducted with acute ischemic stroke patients (modified Rankin Scale =2) and their caregivers. A total of 255 patients and 78 caregivers participated. In-depth interviews were undergone during admission, and at four time points up to 12 months post-discharge. Participants were asked to identify their top concerns across three domains: subjective concerns, health and medical needs, and social welfare services, using single- and multiple-choice formats.

Results: There were shared priorities and differences between patients and caregivers. While the top two ranked need were consistent between patients and caregivers across all three categories, the third ranked need differed, highlighting a discrepancy in priorities. Subjective concerns differed significantly (p0.001); patients were more preoccupied with economic burdens and stroke recurrence, whereas caregivers focused on caregiving responsibilities. Other distinctions included health and medical items (p=0.065) and social welfare services (p=0.08).

Conclusion: This survey highlights areas of overlap and divergence that must be addressed in care planning after stroke. The findings emphasize the importance of addressing overlooked areas. Future community linkage programs should integrate the shared and differing needs of patients and caregivers to support recovery and quality of life.

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Contrast-Enhanced Ultrasound for Post-Stenting Carotid Artery Evaluations: Visualizing Neovascularization and Advancing Restenosis Insights

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Background: Carotid artery stenting (CAS) is an alternative treatment for carotid artery stenosis. Traditional assessments after stenting rely on angiography and Doppler ultrasound. This study explores the potential of contrast-enhanced ultrasound (CEUS) to improve diagnostic accuracy and provide insights into neointima and atherosclerotic plaques in restenosis.

Methods: Five patients with carotid artery restenosis, who regularly attended follow-ups and were on antiplatelet agents and statin, underwent CEUS using Sonovue®. CEUS allowed visualization of the stented segment from the the proximal neointima to the restenosis region, including the presence of neovascularization.

Results: Three patients underwent stenting for symptomatic and two for asymptomatic stenosis, with an average follow-up period of 4.4 years. Intense neovascularization was detected in at least one region of the neointima or plaque in all patients. Three patients showed neovascularization in both areas, while two depicted it in one area. CEUS led to the reclassification of stenosis severity in two patients, shifting from mild to moderate.

Conclusion: CEUS enhances post-stenting evaluations by providing detailed visualization of vascular integrity, particularly in carotid artery restenosis. The detection of intense neovascularization within neointima or restenosis areas highlights the potential role of CEUS in unveiling the pathophysiological mechanism and refining assessments of post-stenting complications.

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Unilateral paramedian midbrain infarct with dissociation between subjective visual vertical and ocular tilt reaction: A case report

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Objective: This case report describes a rare dissociation between subjective visual vertical (SVV) and ocular tilt reaction (OTR) in a patient with right paramedian midbrain infarct, accompanied by features of Parinaud syndrome. The findings provide insights into the pathophysiology of vestibular and oculomotor pathway integration.

Methods: A 20-year-old female presented with sudden-onset diplopia and dizziness. Neurological examination revealed vertical gaze limitation, convergence-retraction nystagmus, and leftward OTR. Imaging studies, including diffusion-weighted MRI, confirmed an acute cerebral infarction in the right paramedian midbrain. The visual vertical test demonstrated a rightward deviation, contrasting with the leftward OTR, indicating a directional dissociation.

Interpretation: OTR and SVV abnormalities are sensitive markers in brainstem lesions and typically deviate in the same direction, reflecting dysfunction of tonic bilateral vestibular inputs stabilizing the eyes and head in roll plane. In this case, the dissociation may result from selective involvement of the ipsilateral vestibulothalamic tract or ascending Deiter's tract lesions.

Conclusion: This case highlights the importance of integrating SVV and OTR findings for accurate diagnosis of midbrain lesions. Recognizing such dissociations enhances understanding of vestibular and oculomotor interactions and informs targeted rehabilitation strategies. Further studies are needed to clarify these mechanisms and improve diagnostic accuracy in midbrain infarct presentations.

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Retrospective Cohort Study on the Impact of Anesthesia Type on TICI outcomes and Clinical Success in Mechanical Thrombectomy for Acute Ischemic Stroke: Our Experience

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The choice of anesthesia during thrombectomy for acute ischemic stroke may influence procedural and clinical outcomes. This study investigates the association between anesthesia type, NIHSS scores, and reperfusion success (TICI scores) to optimize perioperative strategies.

Methods: A retrospective cohort study of 99 patients who underwent thrombectomy between 2022 and 2024 was assessed. Sociodemographic data, NIHSS and GCS scores at admission, post-procedure, and discharge, anesthesia type, complications and mortality were analyzed. Statistical tests included Chi-square, Fisher's exact test, Student's t-test, ANOVA, logistic regression, with significance set at $p \leq 0.05$.

Results: Among the 99 patients, 64.6% were male, with a mean age of 65.1 years (range: 38–84). The largest proportion of patients (61.6%) belonged to the 50–70 age group. Sedation was the most commonly employed anesthesia method (64.4%), followed by general (31.1%) and local anesthesia (4.4%). Sedation was associated with a high rate of successful reperfusion (TICI 2b/3). Successful reperfusion (TICI 2b/3) had higher median NIHSS scores at admission (15.0) compared to those with unsuccessful reperfusion (13.0). Significant improvements in NIHSS scores (14.88 to 8.32, p0.01) and GCS scores (13.57 to 14.64, p0.01) were observed. Complications occurred in 32.6% of cases, and mortality was 7%. Significant independent predictors of mortality included NIHSS-post TE (OR=1.33, p=0.01) and perioperative complications (OR=9.24, p=0.02).

Conclusion: Sedation developed as the predominant anesthesia method with favorable outcomes, while successful reperfusion (TICI 2b/3) was associated with improved clinical outcomes across varying stroke severities. Although anesthesia type did not directly affect reperfusion success, tailored perioperative strategies are critical for optimizing outcomes.

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Successful Management of a Free-Floating Thrombus in the Internal Carotid Artery Using a Direct Thrombin Inhibitor: A Case Report

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Free-floating thrombus (FFT) of the internal carotid artery (ICA) is a rare finding and an uncommon cause of ischemic stroke. Due to the limited number of reported cases and the absence of randomized clinical trials, there is no established consensus regarding the optimal management of carotid FFTs. This report describes the successful resolution of a carotid FFT using a direct thrombin inhibitor in an elderly patient with moderate stenosis.

A 90-year-old male, under regular outpatient follow-up for asymptomatic 80% carotid artery stenosis, was incidentally found to have an FFT during a routine carotid ultrasound. The patient exhibited no neurological deficits on examination and had not previously undergone carotid intervention. He was admitted for close observation and initiated on anticoagulation therapy with the direct thrombin inhibitor, argatroban. By the third day of argatroban therapy, the FFT size had decreased by approximately 50%. After five days, argatroban was transitioned to edoxaban 30 mg daily. A follow-up ultrasound two weeks later demonstrated a further 90% reduction in FFT size Unlike heparin, argatroban does not necessitate routine blood monitoring and offers a favorable safety profile regarding bleeding complications, making it a suitable alternative for acute management of FFTs. This report adds to the limited literature on carotid FFT management and underscores the role of direct thrombin inhibitors, such as argatroban, as a safe and effective treatment option for acute cases.

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Baicalin Protects Neurons from Oxidative Stress and Apoptosis Induced by Glutamate Excitotoxicity in HT-22 Cells

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Baicalin, a flavonoid isolated from Scutellaria baicalensis, has anti-inflammatory, antioxidant, and neuroprotective effects. Glutamate is a representative substance that damages nerve cells by inducing excitotoxicity. We investigated the anti-oxidant and anti-apoptotic effects of baicalin on glutamate-exposed neuronal cells. Mouse hippocampal neuronal cell line (HT-22) were cultured in a general manner, glutamate (5 mM) and/or baicalin (10, 30, 50 uM) were treated on the cells. Baicalin was administered 1 hr before glutamate treatment, and cells were collected 24 hr after glutamate. Reactive oxygen species (ROS) and lipid peroxidation (LPO) analyses were performed to determine the oxidative stress. Western blot and immunocytochemical staining were performed to investigate the expression of bcl-2, bax, and caspase-3. Glutamate induced severe neuronal damage including condensation of the cell shape, baicalin treatment attenuates these morphological changes. Baicalin treatment ameliorates the decrease in cell viability due to glutamate toxicity. Baicalin attenuated glutamate-induced increase of ROS and LPO, and the effect of baicalin on these results was dose-dependent. Glutamate exposure decreased bcl-2 expression and increased bax expression, and baicalin treatment attenuated these changes induced by glutamate. The ratio of bcl-2 to bax was decreased in glutamate exposure, and baicalin prevented this reduction. Baicalin treatment also ameliorated the glutamate toxicity-induced increase in caspase-3. We clearly confirmed that baicalin performs antioxidant and anti-apoptotic functions against glutamate toxicity in neurons. In conclusion, these results suggest that baicalin exerts neuroprotective effects on glutamate toxicity by preventing oxidative stress and inhibiting the apoptotic pathway.

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Cough-Induced Paresthesia Unveiled Cardioembolic Stroke and Septal Aneurysm

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A 61-year-old female was evaluated in the Emergency Department due to transient vision loss in the right eye, following administration of biological therapy for rheumatoid arthritis. Urgent neuroimaging showed no pathological findings, but further investigations were recommended.

Approximately a month later, the patient presented with brief numbness on the left side of the face and the left arm, which occurred during a coughing episode. Neurological examination revealed hypoesthesia on the left side of the nose. Interestingly, the symptoms initially occurred a few days prior to the examination, once again during coughing. A magnetic resonance imaging (MRI) of the brain detected multiple lacunar ischemic strokes in the right hemisphere which were consistent with embolic events, prompting admission to the Neurology Clinic.

Additional diagnostic workup ruled out cerebral aneurysms, significant stenosis, epileptiform abnormalities, antiphospholipid and paraneoplastic syndrome. In order to assess possible cardioembolism, heart echocardiography with Bubble study was performed, suggesting atrial septal aneurysm (ASA), with a potential minor defect and a right-to-left shunt. Finally, transesophageal echocardiogram (TEE) confirmed ASA presence and fossa ovalis duplication, without evidence of a patent foramen ovale. However, the patient was not able to tolerate the complete study, which prevented the Valsalva maneuver.

ASA is widely recognized for its association with an increased risk of adverse cerebrovascular events. Although the diagnostic Valsalva maneuver was not completed, the cough, acting as a natural mimic of the Valsalva maneuver, probably induced intrathoracic pressure changes, which may have triggered a cardioembolic stroke. Based on the findings, anticoagulant therapy was initiated.

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An Unusual Stroke Mimic: A case report

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Background: Ischemic stroke requires rapid assessment due to significant morbidity and mortality. 20% of suspected stroke admissions are mimics. Pneumococcal meningoencephalitis is a rare stroke mimic, with four cases reported.

Case: A 58-year-old female teacher with obesity and anxiety was brought to hospital with sudden-onset inability to speak, right-sided face/arm weakness, and vomiting, witnessed by her class. Examination revealed right-sided facial droop, GCS 9 and NIHSS 12. Initial history was obtained from paramedics/witnesses due to reduced GCS and absence of next of kin. CT head and CTA were normal. She received IV thrombolysis.

However, she subsequently became febrile and developed paroxysmal atrial fibrillation (PAF). Broad-spectrum antibiotics were started while awaiting blood cultures, which, along with a CSF culture from a delayed lumbar puncture, grew Streptococcus pneumoniae.

The patient's GCS gradually improved, her right-sided weakness resolved, but expressive dysphasia persisted. MRI head showed no acute infarction but supported a diagnosis of bacterial meningoencephalitis. Once able to give history, she reported "as if she had a cold" the morning before admission. Recovery was lengthy but uneventful. CT skull base/IAM revealed a focal erosion/deficiency in the left tegmen, likely the infection route. She was discharged after 3 weeks of IV antibiotics and rehab and remains on long-term anticoagulation for primary prevention of PAF-related cardioembolism.

Conclusion: Although rare, pneumococcal meningoencephalitis should be considered in suspected ischemic stroke evaluations. Assessing risk factors is essential but not always feasible. Delays in lumbar puncture due to IV thrombolysis should be factored into recanalisation decisions.

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Safer and More Effective Thrombolytics: Brnoteplase Through Rational Mutagenesis.

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Intravenous thrombolytics have simple administration and are a relatively inexpensive treatment for acute ischemic stroke. However, intravenous thrombolysis achieves a limited recanalization rate (10-40% depending on clot size) and poses a risk of symptomatic intracerebral haemorrhage. In the STROKE Brno consortium (www.strokebrno.cz), we designed novel variants of alteplase using structural bioinformatics, enzyme mining, ancestral sequence reconstruction, and combining favourable mutations from literature. We tested their plasminogen activation, fibrinolysis, and inhibition resistance ability using in vitro and in vivo studies. Selected variants were tested on biophysical arterial occlusion flow and in vivo rat stroke models. The mutants show 400% increased inhibition resistance compared to alteplase, 80-fold higher fibrin selectivity, and up to 400% lower fibrin binding. The most promising mutant, Brnoteplase, shows improved clot penetration and does not exhibit a concentration/efficacy plateau, contrary to alteplase. In the rat model, 2.5 mg/kg Brnoteplase bolus has shown an 87% recanalization rate, compared to 68% in 0.25 mg/kg tenecteplase bolus and 21% in alteplase 0.9 mg/kg bolus + constant rate infusion, while showing 15% occurrence of parenchymal haemorrhage grade 1, compared to 21% in tenecteplase and 35% in alteplase. These favourable properties make Brnoteplase a good candidate for development and clinical use. This project was supported by the project National Institute for Neurology Research (LX22NPO5107 MEYS): Financed by European Union – Next Generation EU. This project was also supported by the European Union's Horizon 2020 Research and Innovation Programme under grant agreements Nos. 857560 and 101136607.

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Primary Antiphospholipid Syndrome as a Cause of Cardioembolic Stroke – Therapeutic Difficulties in Real-life Settings

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Background: Antiphospholipid syndrome (APS) is an autoimmune thrombophilia that can result in ischemic stroke. Recent research suggests that direct oral anticoagulants (DOAC), such as rivaroxaban, and apixaban, are ineffective for the secondary prophylaxis of APS-related stroke, vitamin K antagonists (VKA), such as acenocoumarol, that require periodic INR-based dose adjustments, remaining the recommended approach.

Case presentation: We present the case of a 56-year-old male, with classical modifiable vascular risk factors, admitted to our department for an acute ischemic stroke in the superficial territory of the left middle cerebral artery. The echocardiography revealed a large mobile thrombus in the left ventricle, prompting anticoagulant treatment. Lupus anticoagulant, anticardiolipin antibodies, and anti beta2 glycoprotein I antibodies were intensely positive. The patient had difficult access to INR testing and refused acenocoumarol treatment, so at discharge we decided on secondary prophylaxis with rivaroxaban. After 3 months, the patient had a mild exacerbation of the sequelar right hemiparesis. The brain MRI found several small acute ischemic lesions in the superficial territories of both middle cerebral arteries. The APS workup was once again intensely positive. Acenocoumarol was started, but despite our best efforts, the patient was unable to comply with the INR testing. After 2 months the acenocoumarol treatment was replaced with apixaban and low-dose aspirin. No further clinical events suggestive of stroke occurred over the next 6 months.

Conclusion: Further studies are needed to define better the role of DOAC in patients with APS-related stroke who are unable to use VKA.

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Ischemic stroke in course of dissection of the brachiocephalic trunk.

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A 40-year-old patient was transferred to the Neurology Clinic for mechanical thrombectomy. The patient experienced sudden weakening of the muscle strength of the left limbs and speech disorders of the slurred speech type on the day of admission. CT angiography revealed obstruction of the brachiocephalic trunk and RMCA. The diagnostics were extended to include an MRI of the head. A neurological examination revealed severe left-sided hemiparesis, dysarthria. NIHSS 12 points. The patient was qualified for the procedure according to the DAWN protocol.

In the interview: no chronic treatment, nicotine addiction. The procedure was performed by puncture into the right femoral artery. Braciocephalic trunk obstruction was demonstrated - it was impossible to pass the guidewire through the obstruction. An attempt was made to puncture the radial artery under ultrasound guidance. The right brachial artery was punctured under ultrasound guidance. Obstruction of the M1RMCA was confirmed - the artery was unblocked. Aspiration from the brachiocephalic trunk was performed - in the control angiography it was unblocked. During the patient`s sudden movement the sheath from the brachial artery slipped out.

After the procedure was completed, symptoms of acute ischemia of the right upper limb were observed. A control CT scan of the head revealed a hypodense area of 34mm x 15mm in the deep structures on the right side, angio CT scan revealed the brachiocephalic trunk with features of short dissection with a narrow flow channel. After angiological and anesthesiological consultation, the patient was qualified for brachial artery repair and brachiocephalic trunk stenting.

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Ischemic stroke in course of dissection of the brachiocephalic trunk.

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A case of reversible isolated cognition impairment in meningoencephalitis without abnormal MRI findings

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Most of meningoencephalitis can be showed fever, altered mentality, seizure, muscle weakness and abnormal MRI findings. We report a case of meningoencephalitis with reversible isolated cognition impairment without abnormal MRI findings. The patient showed only isolated cognition impairment without fever and there was no evidence of meningoencephalitis on the contrast enhanced MRI. Although the patient revealed CNS infection with unknown cause in CSF profile, it has some possibilities; 1) Asepticmeningoencephalitis with viral infection, 2)Bacterial meningoencephalitis with early stage, 3)Parasitic meningoencephalitis, 4) Autoimmune meningoencephalitis. Because of the negative findings in autoimmune antibody test, autoimmune meningoencephalitis was less likely. However, it was difficult to diagnose whether it was aseptic meningitis or bacterial meningitis with early stage. After treatment with acyclovir 0.6g for 7days, ceftriaxone 4g, vancomycin 2.5g and Ampicillin 8g for 10 days, confusion and mutism were improved and K-MMSE score was recovered to 18 points. Many reports have been published on meningoencephalitis accompanied by fever, altered mentality, seizure, muscle weakness and abnormal MRI findings respectively. However there have been few cases of meningoencephalitis with isolated cognition impairment and normal MRI simultaneously. If it is a change of consciousness and cognition impairment caused by meningoencephalitis, it can be reversible with proper treatment. Therefore, it is necessary to accurate diagnosis and prompt treatment. Although there is only sudden onset isolated CNS symptom with normal brain MR finding, it is essential to check CSF profile.

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Atypical Location of Diffuse Large B-Cell Lymphoma: A Case Report

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Introduction: Primary central nervous system lymphoma occurs in both immunocompetent and immunocompromised individuals, with diffuse large B-cell lymphoma (DLBCL) accounting for approximately 90% of cases. These lymphomas are commonly located in supratentorial regions, particularly the frontal lobe, thalamus, basal ganglia, and corpus callosum. Primary lymphoma of the skull base is a rare manifestation. Patients typically exhibit symptoms resulting from the compression of critical anatomical structures, such as headache, diplopia, and cranial nerve palsies.

Case presentation: A 42-yr-old female patient began with rightward tongue deviation, diplopia, and right eye esotropia. She was diagnosed with sixth cranial nerve palsy, and a brain MRI was requested. The imaging revealed an infiltrative lesion in the clivus with right-sided predominance, ventral and caudal extension, and involvement of the petrous apex and ipsilateral Meckel`s cave. A transsphenoidal resection of the clival lesion was performed, and histopathology reported DLBCL.

Discussion: Primary clivus lymphoma is an uncommon presentation of non-Hodgkin lymphoma affecting the skull base. This condition poses significant diagnostic challenges due to the overlap in symptoms and radiological findings with more common clival lesions, such as chordomas and meningiomas. Clinically, patients often present with progressive headache, diplopia, and sixth cranial nerve palsy, as observed in our case. Abducens nerve palsy serves as an early and crucial indicator, reflecting the anatomical proximity of the clivus to the nerve.

Conclusions: Our case highlights the importance of including lymphoma in the differential diagnosis of infiltrative skull base lesions, particularly when accompanied by cranial nerve involvement and findings on imaging studies.

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Adult-Onset Phenylketonuria Presenting with Neurological Symptoms: A Case Report

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Introduction: Phenylketonuria (PKU) is an autosomal recessive metabolic disorder caused by phenylalanine hydroxylase (PAH) deficiency, leading to phenylalanine accumulation and neurotoxicity. Early diagnosis through neonatal screening and dietary management significantly reduces neurological and systemic complications. While untreated PKU typically manifests in childhood with intellectual disability, seizures, and motor delays, some cases remain asymptomatic or mildly affected until adulthood, when late-onset neurological symptoms may develop. These include hyperreflexia, movement disorders, ataxia, cognitive decline, and behavioral changes.

Case report: We present a 24-year-old woman with a one-year history of progressive gait instability, cognitive impairment, and behavioral changes. Developmental milestones were normal, but academic performance was poor. Over the past year, short-term memory deficits and behavioral disturbances were reported alongside worsening gait impairment.

Brain MRI revealed diffuse, non-enhancing periventricular white matter lesions with restricted diffusion. This radiologic pattern suggested a metabolic leukodystrophy, with adult-onset metachromatic leukodystrophy and phenylketonuria considered as differential diagnoses. Genetic testing identified two heterozygous pathogenic variants in the PAH gene, confirming the diagnosis of autosomal recessive PKU.

Conclusion: Although PKU is predominantly a childhood-onset disorder, late-onset neurological symptoms can occur in untreated or poorly managed cases. MRI findings, biochemical testing, and genetic analysis are critical for diagnosis. This case highlights the importance of lifelong monitoring and management in individuals with PKU to prevent late-onset complications.

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Long term results for deep brain stimulation for tremor recurrence after focused ultrasound thalamotomy

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Background: MRI-guided focused ultrasound (MRgFUS) thalamotomy has demonstrated efficacy in tremor relief. However, tremor recurrence may occur. For tremor recurrence, deep brain stimulation (DBS) presents a viable alternative. This study reports our experience in preforming DBS following MRgFUS.

Methods: We evaluated four right-handed essential tremor (ET) patients with a mean age of 65 years (range 47-76 years); three of them males, with tremor recurrence 5±5.2 months following MRgFUS. DBS was performed 73.6±54.1 months following MRgFUS. Mean follow up time following DBS was 46±14 months. DBS electrodes were bilaterally implanted in the posterior subthalamic area (PSA) in 2 patients, the ventro-intermediate nucleus (VIM) in one patient and in the PSA traversing the VIM in one patient. Tremor was assessed using Clinical Rating Scale for Tremor questionaire (CRST) and hemi-CRST scores for the treated side. Quality of life was assessed using quality of life in ET questionnaire (QUEST).

Results: At last follow-up visit post-DBS (23.0±14.3), the mean total CRST score was non-significantly decreased compared with pre-DBS (37.0±10.4), and was significantly lower compared with mean pre-MRgFUS score (49.0±6.7, p.05). Hemi-CRST on MRgFUS treated side did not differ post-DBS. QUEST scores did not improve. Adverse events following DBS included persistent gait disturbance (n=3), dysarthria (n=2).

Conclusion: Tremor scores following DBS for tremor recurrence after MRgFUS were significantly improved as compared with pre-MRgFUS. We also found lower tremor scores following DBS, compared to the last pre-DBS follow-up but this did not reach statistical significance. The unfavorable adverse events profile should be considered in patient selection.

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Spinal Dural AVF: From Clinical Suspicion to Endovascular Cure - A Case Report

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Introduction: Spinal dural fistulas (SDAVFs) are rare vascular pathologies of the spinal cord, occurring in 5–10 per 1,000,000 individuals. Typically found in the thoracolumbar region (T6–L2), result in venous hypertension and medullary congestion, causing spinal cord dysfunction. Diagnosing SDAVFs is challenging due to their insidious onset and overlapping symptoms with other neurological conditions.

Case presentation: A 61-year-old male presenting with progressive difficulty walking, lower limb numbness, and urinary retention. On neurological examination the Aminoff Logue scale was G4 U3. Spinal MRI showed medullary edema (T7–L1) and perimedullary vessels. Medullary angiography confirmed a right-sided dural arteriovenous fistula at L2. Endovascular embolization led to significant clinical improvement, with improvement in motor strength and resolution of urinary symptoms. Aminoff Logue scale G3 U1 on discharge.

Discussion: Differential diagnosis included spinal stenosis, discopathy, and polyneuroradiculopathy, supported by elevated cerebrospinal fluid protein. However, the patient's symptom progression, urinary retention, and MRI findings raised suspicion for SDAVF. Typical MRI features include medullary edema, tortuous perimedullary vessels, and hyperintensities on T2-weighted images, often spanning 5–7 vertebral levels. MR angiography can further refine the diagnosis, though catheter angiography remains the gold standard.

Conclusion: Delayed diagnosis, averaging 12–44 months, underscores the importance of early suspicion and advanced imaging in progressive myelopathy cases. This case emphasizes the diagnostic utility of MRI and angiography and highlights the effectiveness of endovascular treatment in improving outcomes for patients with SDAVFs.

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"Carpal Tunnel Syndrome in Patients with End-Stage Renal Disease: A 24-Month Follow-Up Study of 24 Cases"

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Objective: This study aims to investigate the prevalence, clinical progression, and outcomes of Carpal Tunnel Syndrome (CTS) in patients with end-stage renal disease (ESRD) undergoing hemodialysis, over a 24-month period.Methods: A prospective cohort study was conducted involving 24 ESRD patients diagnosed with CTS. Diagnosis was confirmed through clinical assessment and nerve conduction studies. Patient demographics, duration of dialysis, severity of symptoms, and functional status were recorded at baseline. Follow-up assessments were performed at 6, 12, and 24 months, focusing on symptom severity, functional impact, and any interventional treatments received, including surgical release and dialysis access modifications.

Results: Of the 24 patients, 16 (66.7%) were male, with an average age of 59 years. The average duration of dialysis prior to CTS diagnosis was 4.2 years. At baseline, 12 patients (50%) reported severe hand pain and functional limitations. Over the 24-month follow-up, 8 patients (33.3%) underwent carpal tunnel release surgery, which resulted in significant symptom improvement. Nerve conduction studies showed a progressive worsening in 6 patients (25%) who did not receive surgical intervention. A statistically significant correlation was found between the duration of dialysis and severity of CTS (p 0.05). No significant improvement was noted in patients managed conservatively without surgical intervention.

Conclusion: CTS is a prevalent and progressively debilitating condition in patients with ESRD on long-term hemodialysis. Early diagnosis and intervention, particularly surgical release, are crucial in managing symptoms and improving quality of life. This study underscores the need for routine screening for CTS in this high-risk population and suggests that duration of dialysis is a significant risk factor for its severity.

Keywords: Carpal Tunnel Syndrome, End-Stage Renal Disease, Hemodialysis, Nerve Conduction Studies, Surgical Intervention.

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Diabetic Polyneuropathy and vitamin D, correlations to be set

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Introduction: Vitamin D hypovitaminosis has been recently at the center of large studies, especially in the normal functioning of peripheral nervous system. Correlations between low levels of vitamin D and nerve conduction velocities have been studied and discussed, although findings are not uniform. Painful diabetic neuropathy could be a subgroup deemed of scrutiny, while other parameters could serve as a background.

Methodology: Forty patients (20/20 men-women) with diabetic neuropathy of a certain duration (five years) in an age-controlled group (type II diabetic patients aging 50-60 years old) have been tested with electroneurography and responded to VAS (visual analogue scale) in an anonymized form. Values of plasmatic vitamin D were collected and data were correlated with VAS scores.

Results: Severe vitamin D deficiency (levels 4-13 ng/ml) strongly correlated with VAS scores of six points or more (r 0, 7) but not with the decrease of nerve conduction velocities (averaging NCVs of four motor nerves in the lower extremities). The decrease of NCVs was not uniformly distributed (more apparent in male patients) although VAS scores were highly similar in both gender subgroups.

Conclusions: While considering the severity of painful diabetic neuropathy, a diversity of parameters should be taken into account, such as comorbidities, therapeutic compliance, glycemic equilibrium, nutritional status here including any vitamin deficiency. A routine vitamin D check could be helpful and may be included in the diagnostic workup.

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POEMS - A case of plasma cell dyscrasia disguised as CIDP

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POEMS (polyradiculoneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes) is a paraneoplastic syndrome associated with plasma cell disorders. The disease is rare, with an estimated prevalence of 0.3 per 100,000.

A 41 years old female patient, without known prior diseases, is admitted for symptoms progressing over a year consisting of weakness in the distal part of the limbs and painful paresthesias. On examination: symmetric flaccid tetraparesis more severe distally, tactile hypoesthesia, impaired proprioception and painful paresthesias in the lower limbs. On inspection erythema of the face and acrocyanosis were noted.
EMG revealed a severe axonal and demyelinating polyneuropathy with conduction blocks in all four limbs, predominantly in the legs.
Initial lab work revealed a high IgA and mild thrombocytosis. CSF analysis showed albuminocytologic dissociation. A course of IV immunoglobulin followed by rituximab showed no benefit. Extensive follow-up testing revealed monoclonal IgA bands and lambda chains, with highly elevated VEGF (2000 pg/mL). A medullary biopsy showed granulocytic hyperplasia and elevated plasmocytes, with an abnormal kappa/lambda ratio. Imaging revealed one osteosclerotic focal lesion in the right iliac crest and hepatomegaly
The diagnosis of POEMS was based on the following criteria: demyelinating polyneuropathy, IgA monoclonal gammopathy with lambda secretion, high VEGF, osteosclerotic lesion, acrocyanosis, and thrombocytosis.
A course of lenalidomide and dexamethasone was initiated, with clinical benefit yet to be evaluated.

Our case highlights the importance of considering alternative entities in cases of chronic polyneuropathy unresponsive to standard treatment and the need for continued reporting of similar cases to improve treatment strategies.

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Our case highlights the importance of considering alternative entities in cases of chronic polyneuropathy unresponsive to standard treatment and the need for continued reporting of similar cases to improve treatment strategies.

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Charcot-Marie-Tooth Disease Type 1A: A Case Study Highlighting Diagnostic Challenges and Genetic Implications in a Family with a History of Polyneuropathy

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Background: Charcot-Marie-Tooth (CMT) disease, a hereditary motor and sensory neuropathy, presents a diagnostic challenge due to overlapping clinical features with acquired neuropathies and hereditary spastic paraplegia-plus syndromes (SPG-plus).In Georgia, there are only a few genetically established cases. Presented Familial case of CMT Type 1A illustrates the importance of genetic testing and early diagnosis in patients with progressive peripheral neuropathy and a family history of similar symptoms.

Case Description: A 54-year-old male presented with a several-year history of weakness in the lower extremities, atrophy of tibial muscles, impaired tactile and pain sensation, poor fine motor coordination, and fatigue.

Neurological examination revealed spastic paraparesis, distal neuropathy, and sensory disturbance with pathological reflexes. In addition to progressive walking difficulty, the patient also experienced urinary incontinence. Chronic sensorimotor polyneuropathy was confirmed by EMG, alongside MRI findings of lacunar gliosis. Family history was significant, as both his sons reported numbness in their legs, confirmed by EMG revealing the same data as the father`s. Genetic neuropathy was suspected, prompting genetic testing for CMT.

Results: Confirmed a duplication in the PMP22 gene, diagnostic for CMT Type 1A. This clarified the underlying etiology of the patient's and his sons' progressive neuropathy.

Conclusion: This case highlights the critical role of genetic analysis in diagnosing hereditary neuropathies like CMT, particularly in patients with family histories of polyneuropathy. Early diagnosis facilitates tailored management strategies, genetic counseling, and surveillance for disease progression.

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Clinical approach for diagnosing familial cortical myoclonic tremor with epilepsy - FCMTE

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Background: Familial cortical myoclonic tremor with epilepsy (FCMTE) is a rare disease with a benign course characterized by myoclonic tremor and rare epileptic seizures. It is often a diagnostic challenge because genetic studies are not fully established. Linkage analyses were performed with microsatellites encompassing the two known loci (8q 23.3-q24.1 and 2p11.1-q12.2). Besides this, it is not always possible to do genetic testing. Diagnosis is based on the clinical and electrophysiological findings.

Discussion: We report a 61-year-old woman with jerky movements and epileptic seizures that debuted six months before admittance. MRI and EEG were normal. Family history is positive as the patient's sister has a similar clinical phenotype. Involuntary movements were distributed in the upper body and head, also propriospinally. Jerks were fast, had high frequency and repetitive manner, and had some kind of rhythmicity. These jerks were expressed in resting positions including sitting and supine conditions, as well as standing and walking. Jerks were exaggerated by stress and postural changes. Intensity and frequency were rising while walking. The clinical scenario includes 3 episodes of losing consciousness with vocalizations and stiffness of limbs. Apart from myoclonus neurological exam revealed only mild intention tremor. The patient had a good response to levetiracetam for seizures and clonazepam for myoclonic tremor.

Conclusion: In the absence of genetic data, thorough history taking, neurological examination, and paraclinical data together with positive treatment response give us the opportunity to diagnose this rare disorder.

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Adolescence Onset Primary Coenzyme Q10 Deficiency - 4: A Case Report

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Introduction: Primary coenzyme deficiency - 4 (COQ10D4) is an autosomal recessive disorder characterized by onset of cerebellar ataxia and exercise intolerance. Some affected individuals develop seizures and have mild mental impairment, indicating variable severity.

Methods: A brief description of the Adolescence Onset Primary Coenzyme Q10 Deficiency - 4 in two brothers in North Macedonia.

Results: We report a case where the pathogen variant in the COQ8A gene is homozygous in two adult brothers. Autosomal recessive inheritance is consistent with the COQ10 deficiency transmission pattern in the families. In this case, genetic analysis showed the same variant was present in both parents. From a neurological perspective, cerebellar ataxia, head tremor, positive Gowers`s sign, proximal muscle weakness, and pseudohypertrophy of the calf muscles clarify the clinical framework. Both brain magnetic resonance imaging (loss of the white matter, cerebellar atrophy, and thinning of the corpus callosum) and electromyography confirmed the clinical diagnosis. As well, abnormal serum creatine kinase levels were monitored.

Conclusion: By highlighting the significance of early detection of potentially treatable COQ8A mutations, these case report overviews support healthcare professionals in better recognising the symptoms of this condition.

Keywords: adolescence onset; primary coenzyme Q10 deficiency - 4; neurological perspective; early detection; proximal muscle weakness.