P.089

Multiscale analysis of mesial temporal lobe epilepsy: Anatomo-Electrophysio-pathologic differentiation

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Background: Mesial temporal lobe epilepsy (mTLE) is a heterogenous condition with variable post-surgical outcomes. Combining high resolution magnetic resonance imaging (MRI), stereoelectroencephalography (SEEG) and histology may establish different subtypes of mTLE. Methods: Retrospective analysis of patients with mTLE with 1) SEEG Patterns 2) MRI 3) Post temporal lobectomy tissue analysis 4) Engel Classification. *HippUnfold* method was used to segment hippocampus on MRI. Results: Of 109 patients investigated with SEEG, 11 patients were analyzed so far. Low voltage fast activity was seen in 215 seizures, low-frequency periodic spikes in 21, sharp activity at <13 Hz in 58, rhythmic spike sharp wave activity in 86, and other types were less frequent. MRI revealed unilateral mesial temporal sclerosis (MTS) in 6 (54.55%), bilateral MTS in 2 (18.18%), and was normal in 3 (27.27%) patients. Histopathology showed ILAE grade I in 3 (37.5 %), II in 4 (50 %), IV in 1 (12.5%) patient. 63.63% had Engel Class I at 6 months. HippUnfold analysis and SEEG electrode coregistration was done in one patient and will be attempted in the rest. Conclusions: Our study highlights a strong correlation between SEEG findings and histological analysis in mTLE. A multidimensional classification will help predict long term outcomes.

P.090

Investigating deep brain stimulation parameters for drug resistant epilepsy treatment: a literature review

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Background: Drug-resistant epilepsy (DRE), defined by persistent seizures despite appropriate anti-seizure medication trials, affects about one-third of individuals with epilepsy. Deep brain stimulation (DBS) has emerged as a promising avenue for improved seizure control. This project reviews existing publications to better understand the neuromodulation parameters used in DBS, aiming to inform clinical decisions on optimizing treatment parameters in patients living with DRE. Methods: A comprehensive literature search of PubMed and Google Scholar was conducted using the keywords "DBS," "epilepsy," and "parameters." Only original studies reporting specific stimulation parameters were included, with meta-analyses and review papers excluded. A weighted Pearson correlation, using study sample size as the weight, examined frequency, pulse width, seizure reduction, and responder rate. Results: So far, 28 studies (1997-2024) have been reviewed, encompassing a total of 1,054 patients, with study size ranging from 1-250 patients. Electrode targets included the hippocampus, ANT, amygdala, centromedian nucleus, and STN. DBS frequencies ranged from 60–333 Hz, and pulse widths from 40–450 μs. Pearson correlation results suggest moderate frequencies (130–145 Hz) and wider pulse widths (300–450 μs) correlate with better seizure reduction and higher responder rates. Conclusions: These results support a formal meta-analysis to further investigate neuromodulation parameters to improve outcomes for DRE patients.

Neurocritical Care

P.091

Parameterized short-segment EEG improves neurological recovery prediction in patients with severe brain injury

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Background: Predicting neurological recovery in patients with severe brain injury remains challenging. Continuous EEG monitoring can detect malignant patterns but is resource-intensive, and its role in long-term functional outcome prediction is unclear. This study evaluates the utility of parameterized short-segment EEG, acquired via EEG cap, in predicting neurological recovery. Methods: We analyzed short-segment high-density EEGs from 42 patients in the NET-ICU cohort with acute neurological injury. EEGs were pre-processed into standard clinical formats and parameterized using five visual EEG features associated with outcome prediction. Random Forest Classifier (RFC) models were trained and cross-validated to predict recovery of responsiveness (following 1-2 step commands during or after ICU admission) using: EEG features alone; clinician prediction combined with EEG features. Results: EEG-based prediction outperformed clinician bedside assessment (AUC ROC: 0.80 vs. 0.67) under the RFC model. Combining clinician Glasgow Outcome Scale–Extended (GOSE) scores with EEG features improved overall predictive performance (AUC ROC: 0.91). Conclusions: Standardized EEG features obtained using EEG caps can improve the accuracy of neurological recovery predictions in patients with acute severe brain injury. This suggests that automated extraction of background brain signals has the potential to provide clinically meaningful prognostic information in critical care settings, enhancing accessibility and resource efficiency.

Neuromuscular Disease and EMG

P.093

A case of refractory NF155 Paranodal CIDP with near-complete spontaneous recovery

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Background: CIDP is a rare immune-mediated demyelinating neuropathy that has significant phenotypic variability. A unifying

immunopathological mechanism remains elusive, likely due to etiological heterogeneity among the variant presentations. This is best exemplified by the identification of nodal/paranodal antibodies, such as neurofascin 155, in a subgroup of CIDP patients who present with a distinct phenotype. Methods: We present the case of a 39-year-old male who presented with a 2-year history of progressive stocking-glove sensory loss and sensory ataxia. Electrodiagnostics confirmed an acquired demyelinating neuropathy, with serum anti-NF155 IgG4. His case was refractory to standard immunomodulatory therapy, including adequate trials of IVIG, steroids, azathioprine, and rituximab. He also had a non-therapeutic trial of PLEX, methotrexate, and tacrolimus. Results: After cessation of all immunomodulatory therapy for 2 years, he had spontaneous remission of his CIDP and near-complete resolution of electrodiagnostic/clinical abnormalities. Conclusions: This case provides insights into the natural history of NF155 "paranodalopathy" and highlights a unique case of supra-refractory CIDP which underwent spontaneous remission with near-complete resolution. Delayed effect from rituximab was posited as a contributor, however, the patient had no clinical or electrophysiological improvement 20-months after initiation of anti-CD20 therapy. Current data suggests the majority of CIDP patients respond to rituximab within 6-12 months.

P.094

A phase 1, multicenter, randomized, placebo-controlled, multiple ascending dose study to evaluate the safety and tolerability of AMX0114 in ALS (LUMINA)

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Background: Axonal degeneration has been recognized as a key early contributor to the clinical presentation and pathogenesis of amyotrophic lateral sclerosis (ALS). Activation of the calcium-dependent cysteine protease calpain-2 is considered a critical effector of axonal degeneration. Based on evidence supporting a potential benefit of calpain-2 modulation in ALS and other neurodegenerative diseases, Amylyx developed AMX0114, an antisense oligonucleotide (ASO) inhibitor of calpain-2. This phase 1 study will assess the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of AMX0114 in people with ALS. Methods: LUMINA is planned to be conducted at ~15 sites in North America enrolling approximately 48 participants randomized 3:1 to receive AMX0114 or placebo. After study completion, an open-label extension study of AMX0114 will be implemented if data supports a positive benefit-risk profile. Results: The primary endpoints of the study include the incidence of adverse events (AEs), serious AEs, and dose-limiting toxicities. Secondary and tertiary endpoints include PK measurements (plasma and cerebrospinal fluid [CSF] levels of AMX0114), PD biomarkers, and functional measures of ALS progression. Conclusions: LUMINA is a first-in-human study evaluating the safety, tolerability, PK, and PD of AMX0114, the first ASO targeting calpain-2 in adult participants with ALS. Enrollment is planned to begin in Canada in early 2025.

P.096

Final pooled analysis of efficacy and safety of rozanolixizumab cycles in patients with generalised myasthenia gravis: MycarinG and open-label extension studies

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Background: In the Phase 3 MycarinG study (MG0003/NCT03971422), one 6-week cycle of rozanolixizumab significantly improved myasthenia gravis (MG)-specific outcomes versus placebo. After MycarinG, patients could enrol in open-label extension studies (MG0004 then MG0007, or MG0007 directly). Methods: In MG0004 (NCT04124965), patients received once-weekly rozanolixizumab 7mg/kg or 10mg/kg for ≤52 weeks. In MG0007 (NCT04650854), after a cycle of rozanolixizumab 7mg/kg or 10mg/kg, subsequent cycles were based on symptom worsening at the investigator's discretion. Pooled data are reported across MycarinG, MG0004 (first 6 weeks) and MG0007 (final data) for patients receiving ≥2 symptom-driven cycles (efficacy; ≤13 cycles) or ≥1 cycle (safety). Results: 196 patients received ≥1 rozanolixizumab dose of whom 129 received ≥2 symptom-driven cycles (7mg/kg: n=70; 10mg/kg: n=59). Treatment response was maintained from Cycles 1–13: mean change from baseline to Day 43 in MG-Activities of Daily Living score ranged from -3.2 to -4.9 (7mg/kg) and -3.2 to -6.7 (10mg/kg). Quantitative MG and MG Composite scores also improved. Treatment-emergent adverse events (TEAEs) did not increase with repeated cyclic treatment, and most were mild/moderate; the most common event was headache. Conclusions: Rozanolixizumab showed consistent improvements across MG-specific outcomes up to 13 cycles and repeated cyclic treatment was generally well tolerated. Funding: UCB.

P.098

Does single fiber EMG (SFEMG) pair number influence the outcome of patients initially referred for possible myasthenia gravis (MG)?

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Background: Analysis of 20 pairs is the traditional standard when using SFEMG to diagnose MG. Some studies show that fewer pairs are needed if results are normal. We examined what impact this might have on long-term outcomes. Methods: Hospital charts of 239 consecutive patients who underwent SFEMG between January 2011, and July 18th, 2024, were reviewed. Results: 201 patients were identified; 128 had normal SFEMGs. Of the patients with normal SFEMGs, 58 (45.31%) had 12 pairs observed and 69 (53.91%) had 20 or more pairs observed. In the 12 pair group, 1(1.72%) patient had delayed MG diagnosis, and 2 (3.45%) patients were referred for repeat SFEMGs; in the 20 or more group,