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Abstracts

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Bee Venom Nanoliposomes to Potentiate In Vivo Antioxidant and Anti-Inflammatory Responses as an Adjuvant Strategy for the Prevention of Post-Traumatic Epilepsy Using a Novel Fluid Percussion Model

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Traumatic brain injury (TBI) is a major cause of morbidity and mortality in young adults and a significant risk factor for the development of post-traumatic epilepsy (PTE). The associated oxidative stress and neuroinflammation have motivated the search for neuroprotective and antiepileptogenic therapies. Bee venom contains bioactive compound, such as melittin, apamin, adolapin, and enzymes like phospholipase A2, that exhibit antioxidant and anti-inflammatory properties. This study aimed to develop and evaluate two strategies: (1) a controlled-release system based on nanoliposomes encapsulating bee venom, and (2) an automated, low-cost device for TBI induction in a murine model using a hydropneumatic percussion system. Nanoliposomes were synthesized via lipid film hydration with ultrasound assistance and evaluated under simulated oral, gastric, and intestinal digestion. The formulation showed high encapsulation efficiency (91.9%) and sustained release (66.4% at 24 h), with the oral phase yielding the highest melittin release (90.8%) and antioxidant activity. Hemocompatibility assays revealed erythroprotective effects, with hemolysis inhibition varying by blood group (69.7% in A RhD^+ to 28.3% in O RhD^-). The system also exhibited anti-inflammatory activity under thermal hemolysis (91.9%) and hypotonic stress (60.6%), with a blood compatibility of 72.9% at 30 µg/mL and LD_{50} of 87.3 µg/mL.

For TBI induction, the device integrated sensors, a PLC, and touchscreen control, regulating water volume, pressure (up to 3.8 atm), and impact duration (20–100 ms). Male Wistar rats were assigned to Sham (n=21) and TBI (n=24) groups. TBI was induced at 1.0 ± 0.22 atm for 50 ms. The device showed reproducible parameters. Post-TBI, 25% mortality, 72% apnea (mean 17 s), and delayed righting reflex (12 s) were observed. Somatosensory deficits were present in 41.7% of TBI animals (NEUROSCORE-Plus).

This study provides a standardized model for TBI induction and a promising bee venom-based delivery system with potential for PTE treatment. Future work will focus on in vivo validation, dosage optimization, and enhanced targeting for neuroinflammatory diseases.

Long-term Effectiveness of Vagus Nerve Stimulation in Pharmacoresistant Epilepsy: A Retrospective Analysis

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Neurostimulation techniques, including vagus nerve stimulation (VNS) and deep brain stimulation of the anterior thalamic nuclei (ANT-DBS), represent important treatment options for patients with pharmacoresistant epilepsy. Despite their widespread use, the inability to predict treatment response prior to implantation remains a significant clinical challenge. The aim of this project is to identify potential biomarkers that can reliably predict the efficacy of neurostimulation by analyzing clinical, electrophysiological, and therapeutic data. We conducted a retrospective analysis of patients treated with VNS at our center, collecting data on seizure frequency, epilepsy characteristics, and medication regimens. So far, data from 170 patients have been processed, representing a subset of our total VNS-treated cohort. Responders were defined as patients achieving at least a 50% reduction in seizure frequency compared to baseline. Preliminary results show that 56% of patients were responders at one year, with a marked increase in the early years—rising to 68% at three years and 79% at five years. The proportion of responders continued to gradually increase with long-term follow-up, exceeding 84% at ten years. Complete seizure freedom (100% reduction) was achieved in 28 patients (17%). The average time to initial ≥50% response was 9 months, with 54% of patients responding by that timepoint. These early findings highlight the progressive and sustained efficacy of VNS, as well as the potential for identifying early predictors of treatment response. Once complete, this study may help improve patient selection, reduce unnecessary procedures in non-responders, and deepen our understanding of neuromodulatory mechanisms in epilepsy.

Folate transfer across the placenta during late pregnancy in women with epilepsy: a cross-sectional, two-center study

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Background: Antiseizure medications (ASMs) are linked to adverse pregnancy outcomes and reduced maternal folate levels. However, maternal serum folate may not reliably reflect fetal folate supply, as ASMs can impair placental folate handling. This study aimed to assess folate transfer at birth in pregnant women with epilepsy versus controls and identify influencing factors.

Design: A cross-sectional, two-center study was conducted from April 2022 to May 2024. Participants included 22 pregnant women with epilepsy who received ASMs, 10 untreated women with epilepsy, and 19 control individuals without epilepsy. Maternal venous and umbilical cord blood samples were collected at delivery. Folate levels were measured using chemiluminescence assay and ASM concentrations were analyzed in maternal and cord serum. Statistical analyses included Kruskal-Wallis, Mann-Whitney, Fisher's exact tests, linear regression, and Michaelis-Menten kinetics.

Results: Maternal and neonatal characteristics were similar across groups, except for higher cesarean rates among controls (p.001). Folate deficiency was observed in 35% of women with epilepsy and 42% of controls. Median cord/maternal folate ratios were 1.51 (95% CI 0.92–6.35; n=17) in ASM-treated women and 2.02 (95% CI 1.69–3.71; n=19) in controls. In epilepsy cases, placental folate transfer followed saturable kinetics (Cmax=131.1 ng/mL; Km=32.6 ng/mL; R^2=0.70). In term deliveries, model predictability improved (Cmax=125.2 ng/mL; Km=41.1 ng/mL; R^2=0.78).

Conclusion: Fetal folate supply depends largely on maternal levels and is saturable in epilepsy. Frequent maternal folate deficiency supports the need for ongoing supplementation and monitoring during pregnancy.

The critical role of sleep deprived EEG in Diagnosis.

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This presentation discusses an intriguing case of a 38-year-old patient who presented at the ER of Regional Hospital of Lezha, with episodes of transient loss of consciousness, each lasting 5-6 seconds and accompanied by epigastric prodromal symptoms, including nausea and sweating. The patient reported a total of eight episodes since September 2023. Both the brain MRI, and standard EEG were normal, making our case more interesting and challenging.

However, a sleep deprived EEG revealed the presence of epileptic sharp waves in the left temporal lobe, offering additional details regarding the etiology of our patient symptoms. This case emphasizes the importance of sleep-deprived EEG as a valuable diagnostic method in identifying epilepsy, particularly when initial imaging and standard EEG findings fail to help us in diagnosis.

By presenting this case, I aim to draw attention among clinicians about the necessity of considering sleep deprived EEG in the evaluation of patients with unexplained loss of consciousness.

Antiepileptic Drug Withdrawal and Its Differential Impact on Scalp and Intracranial EEG: Insights from Advanced Data Analysis

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Background: Antiseizure-medication (ASM) tapering during presurgical monitoring perturbs cortical networks; yet it remains unclear whether scalp video-EEG (VEEG) and depth-sampling stereo-EEG (SEEG) register those pharmacodynamic shifts with comparable fidelity.

Objective: Quantify modality-specific biomarker changes across graded ASM exposure and assess drug-modality interactions.

Methods: We retrospectively reviewed patients who underwent Phase-1 VEEG and Phase-2 SEEG. All experienced ASM dose changes for diagnostic tapering or treatment adjustment. Exact timestamps of each reduction recorded, enabling analyses anchored to the moment of dose change. Using advanced signal-processing, deep-learning, and machine-learning techniques, we assessed pharmacological effects on EEG biomarkers—including (1) interictal spike rate, (2) alpha/beta power, (3) high-frequency activity, (4) band-limited synchrony, and (5) network functional connectivity—across both modalities. Analyses focused on short EEG epochs to capture dynamic, real-time neurophysiological responses.

Preliminary observations: Depth electrodes reveal focal, dose-dependent shifts in high-frequency power and delta suppression, whereas scalp recordings exhibit broader changes in background rhythms with limited high-frequency sensitivity. Correlations between drug level and spike rate appear stronger in SEEG than in VEEG. Additional data from further patient recordings are currently being processed and will be presented at the meeting.

Significance: Confirmed findings could (i) enable biomarker-guided taper schedules that minimise seizure risk and monitoring duration, (ii) provide modality-specific markers for precision polytherapy, and (iii) deepen mechanistic insight into how different ASM classes remodel cortical and subcortical networks. Leveraging a rare paired VEEG-SEEG dataset with rigorous signal analysis, this study reframes routine monitoring as a platform for personalised pharmacodynamic profiling and informed surgical planning.

Progressive cortical and hippocampal atrophy after status epilepticus: a prospective longitudinal MRI study

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Purpose: Status epilepticus (SE) is a neurological emergency that leads to neuronal injury and increased mortality. We investigated longitudinal trajectories of cortical thinning and hippocampus atrophy following SE using serial brain MRI, an established biomarker of neurodegeneration in epilepsy.

Method: This longitudinal prospective study analyzed 281 MRI scans from 112 participants, including 39 individuals with SE who underwent acute brain MRI within 48h of SE and up to 4 follow-up scans, and 47 controls with drug-resistant focal epilepsy (DRFE). SE semiology categorized SE into convulsive (CSE, n=17), non-convulsive (NCSE, n=20) and convulsive to non-convulsive SE (CSE-NCSE, n=2). Cortical thickness was measured via a surface-based framework together with hippocampus volumetry in structural serial MRI scans in all participants, whereas the rate of thinning/atrophy was compared between groups using mixed effect models. Analysis was performed relative to the side of seizure onset (ipsilateral vs. contralateral).

Results: Groups differed in age [SE 59±18 vs. DRFE 31±12 years, p.001] and interval between baseline and last scans (SE 149±214 days vs. DRFE 414±394 days, p.001]. Widespread accelerated cortical thinning of the ipsilateral hemisphere was observed in SE (p.001), while hippocampal atrophy was faster bilaterally (ipsilateral p.001, contralateral p.01) as compared to DRFE. Both CSE and NCSE were associated with accelerated cortical thinning (both p.001) and hippocampal atrophy (CSE: ipsilateral p.001, contralateral p.001; NCSE: ipsilateral p.01, contralateral p.05) when compared to DRFE. SE duration independently contributed to an accelerated cortical thinning (p0.001) and ipsilateral hippocampal atrophy (p.01).

Conclusions: SE is linked to widespread irreversible progressive brain damage, exceeding that seen in refractory focal epilepsy. Despite SE semiology and duration influencing the extent of atrophy, NCSE is similarly associated with accelerated neurodegeneration. Our findings highlight the importance of prompt SE termination to mitigate brain injury and further underscores the relationship between prolonged seizure activity and neurodegeneration.

Status epilepticus in elderly: an Italian multicenter, retrospective, real-world study.

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Introduction: Status Epilepticus (SE) is a neurological emergency with a mortality risk of around 20%. SE onset occurs in all ages, including the elderly. Clinical hallmarks, as well as the therapeutic approaches of SE when applied to the elderly, have not been exhaustively explored in the literature.

Methods: in this retrospective, multi-center, real-world study, patients aged75 were selected from two third-level epilepsy centers between 2011 and 2023. Demographics, clinical and SE four diagnostic axis (i.e., age, semiology, etiology and EEG correlates) and therapeutic interventions were collected. GCS, STESS, EMSE, and CARING scales were evaluated as outcome predictors.

Results: 87 patients (age: 83 ± 6, 28 male) were included. Non-convulsive SE with acute etiology was mainly described. Patients were treated with a mean number of 2.7±1.5 drugs. First-line treatment consisted of diazepam (mean dose: 10.4±3.3 mg) in most patients, followed by levetiracetam (mean dose: 1815.8±931.1 mg). Among the ASM, levetiracetam, valproic acid, phenytoin, and lacosamide were most employed. Thirty-three patients developed a refractory SE, and 32 patients died of SE. Compared to survivors, patients who died for SE showed an increased prevalence of cardiological comorbidities (p=0.03). Refractoriness was not a predictor of mortality (r=0.21). STESS (p=0.002), EMSE (p=0.01) and CARING (p=0.01) scales resulted as good outcome predictors tools.

Conclusions: SE is associated with a great mortality in the elderly. Treatment strategies generally consist of benzodiazepine and ASM. Anesthetics are less employed. Commonly used prognostic scales (i.e., STESS and EMSE) show good reliability. The CARING scale can be employed in elderly patients as an outcome predictor tool.

The phenotypic presentation of adult individuals with IQSEC2-related neurodevelopmental disorders

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Purpose:
This study aims to describe the adult evolution of *IQSEC2*-related developmental and epileptic encephalopathy (DEE).

Method:
We retrospectively reviewed clinical data from five patients with *IQSEC2*-related DEE followed at the Danish Epilepsy Center.

Results:
We report the electro-clinical phenotypes of five adult patients (4 males, 1 female, all 16 years). Male patients had seizure onset in early childhood (post-infancy), while the female patient developed seizures during adolescence. Seizures were polymorphic, initially presenting as generalized tonic-clonic. Three male patients shared a severe clinical course and similar EEG features, notably subcontinuous bifrontal monomorphic delta activity with epileptiform discharges. One male patient showed a milder phenotype and normal adolescent EEG; his variant may generate a premature stop codon escaping nonsense-mediated decay, possibly explaining the attenuated presentation. The female patient had no epileptiform EEG abnormalities. Most patients had neurodevelopmental delays; three males were nonverbal, and three achieved independent walking, though one later experienced motor regression. The female patient is ambulatory with sparse language. No structural epileptogenic lesions were identified on neuroimaging. Autistic spectrum disorder-like features were observed in four patients, and drooling in three.

Conclusion:
IQSEC2-related DEE shows variable progression into adulthood, with some patients presenting a milder phenotype. Genotype-phenotype correlations may be influenced by variant impact on protein function. Frontal delta activity may indicate a more severe clinical presentation.

The Role of Adult Neurogenesis during Epileptogenesis in a Viral Encephalitis-induced Seizure Model

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Neurogenesis, the generation of new nerve cells, is disrupted in traditional rodent epilepsy models, and altered cell maturation and migration contribute to hyperexcitability and cognitive impairment. Very little is known about the impact of encephalitis-derived seizures on neural stem cells (NSCs) and their differentiation after infections of the central nervous system (CNS), although CNS infections are one of the major causes of seizures. We are aiming to identify treatment windows for modulating neurogenesis to modify epileptogenesis after CNS infection.

The Theiler's murine encephalomyelitis virus (TMEV) model is a translational mouse model that simulates infection-triggered acute, and chronic, unprovoked seizures. An intracortical, unilateral injection of the Daniel's strain of Theilervirus induces seizures in 50-75% C57BL6 mice within the first week, and about 25% of mice develop chronic epilepsy. Mice were sacrificed at 7-, 14-, 28- and 90 days post infection (dpi) to evaluate neurogenesis in the subgranular layer of the hippocampal dentate gyrus.

TMEV infection rapidly depleted subgranular immature neurons (DCX+), with mice experiencing seizures demonstrating a more pronounced reduction in neuronal progenitor cell density. Additionally, seizures induced ectopic migration of surviving neuronal progenitors at 14 dpi. On the contrary, proliferating microglia and astrocytes were significantly increased in TMEV infected animals depending on the timepoint. Ongoing long-term fate tracking of progenitor cells by BrdU labelling in 28 dpi and 90 dpi animals will reveal the fate and migration patterns of NSCs within the hippocampus over the disease course, and determine their role in seizure development.

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Quantification of the effect of antiseizure medication (ASM) on interictal epileptiform discharges (IED) in idiopathic generalized epilepsy (IGE)

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Purpose:

Semi-automated quantification of the effect of ASM on IEDs based on long-term video-EEG (LT-VEM) recordings of patients with IGE who underwent changes in ASM dose during LT-VEM.

Method:

IED detection was performed using the encevis 1.11.3 software (AIT) with subsequent verification of the detections by two certified EEG experts.

The cumulative ASM daily dose was calculated in relation to the WHO Defined Daily Dose (DDD). The day with the lowest and highest cumulative dose according to the DDD was then determined. The IED rate per minute from 20:00 to 08:00 was compared using paired parametric statistical methods.

Results:

39 LT-VEM recordings from IGE patients with a total of 3223 hours of EEG were included. 136385 IEDs were detected. The median cumulative daily dose in DDD was 0.62 on the day of the lowest ASM dose and 2.1 on the day of the highest dose.

34 of 39 (87.18%) IGE patients showed a lower IED rate per minute on the night with the highest ASM dose compared to the night with the lowest dose. The median IED rate of the night with the lowest ASM dose was 0.15 and the night with the highest was 0.05 IEDs per minute. The difference was highly significant in comparison (P 0.01). The median reduction in the IED rate was 71% (range 5%-100%).

Summary:

In 87.18% of the examined patients there was a reduction in the IED rate when comparing the night with the lowest and highest cumulative ASM daily dose.

Psychotic manifestations of lesional right temporal epilepsy: A case report of diagnostic challenge in a pregnant patient

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Epilepsy, especially temporal lobe epilepsy, can be associated with psychotic symptoms, manifested as ictal or postictal psychosis.

A 24-year-old patient, G1P0 in the 14th week of her pregnancy, was hospitalized with frequent attacks of generalized tonic-clonic seizures with eye fixation, jerky movements of the trunk and limbs, and foam/saliva coming from the mouth. These episodes lasted around 2-3 min, were associated with cyanosis and ictal involuntary urination. The patient was confused postictally, tired, and complained of muscle aches. Otherwise, the neurologic examination was normal between the attacks. Treatment with Lamotrigine 25 mg/ day was initiated.

She had been diagnosed with Idiopathic Generalized Epilepsy at the age of 12, but the patient was noncompliant with the treatment with Carbamazepine and Clonazepam 0.25 mg.

After two days, the patient manifested episodes with mannerisms and facial grimacing, “the feeling of falling out of the body”, “tongue drop”, “bone loss sensation”, “the feeling of leaving the body”, visual hallucinations (seeing snakes in the room, seeing blood in the room, she was bleeding) associated with frightened reactions. She was afebrile. Blood tests showed no alteration in glucose, renal, hepatic, or thyroid function, and no electrolyte disturbance.

Interictal EEG was normal. The MRI showed a right cortical temporal lesion. Increases in dose of Lamotrigine and acute treatment with benzodiazepines lead to symptom cessation.

In conclusion, seizures with nonmotor manifestations pose a major diagnostic challenge. They should be distinguished from the psychosis in pregnancy and the psychiatric comorbidities in epilepsy to avoid unnecessary treatment with antipsychotics.

A diagnostic dilemma: Frontal lobe epilepsy or psychogenic non epileptic seizures? The complexity of EEG interpretation.

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The typology of seizures can be hard to diagnose because it´s difficult to tell the difference between epileptic seizures and non- epileptic seizures that are caused by psychological factors. This case is about a 50-year-old man from Kukes, Albania, who was thought as a psychiatric patient because of his history and the clinical manifestations of the epileptic crises. However, after further evaluation and observation, and after an EEG was performed, the patient was diagnosed with Frontal Epilepsy.
During his episodes, the patient showed muscle stiffening and jerking movements, pelvic thrusting and eye closure, which are often seen in psychogenic seizure. These signs, along with the lack of confusion afterwards and the presence of psychological stress, made us consider our patient as a psychiatric one. But in the EEG, frontal theta waves were seen.

It´s very important to distinguish between true epileptic seizures and psychogenic seizures because it affects how the patient is treated and managed.
This case highlights the importance of differential diagnosis in seizure disorders. Clinicians should use a multidisciplinary approach, considering both neurological and psychological factors, to avoid misdiagnosis that could lead to inappropriate treatments. Getting the right diagnosis, not only helps to take better care of the patient, but also lowers the risks that come with psychogenic disorders. Further research and education are needed to improve recognition of PNES, particularly in regions where access to specialized seizure disorder services may be limited.

Keywords:
Psychogenic Non-Epileptic Seizures, Epileptic Seizures, Differential Diagnosis, Case Study, Albania, Seizure Disorders

Use of Cenobamate in Pediatric Patients with Epileptic and Developmental Encephalopathy related to SCN2A/SCN8A Mutations: A Preliminary Analysis

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Background and Objectives

Mutations in the SCN2A and SCN8A genes, which encode subunits of sodium channels, cause early-onset drug-resistant seizures and delayed psychomotor development. Cenobamate has a dual mechanism of action: it acts as a positive allosteric modulator of GABA_A receptors and blocks sodium currents, thereby helping reduce excitatory neurotransmission.

We report the efficacy and tolerability of cenobamate in patients with epileptic and developmental encephalopathy due to SCN2A and SCN8A mutations.

Methods

Clinical data were retrospectively collected from four pediatric patients with epileptic and developmental encephalopathy: two with SCN2A mutations and two with SCN8A mutations.

Results

We enrolled three females and one male, aged between 8 months and 8 years. All patients had experienced seizure onset within the first year of life. The most frequent seizure types were epileptic spasms, tonic seizures, focal seizures and generalized tonic-clonic seizures. Multiple antiseizure medications were attempted, with the most common combination being cenobamate with carbamazepine and clobazam, used by three out of four patients. All subjects reported a reduction in seizure frequency and intensity, as well as decreased use of rescue medications. No adverse effects were observed that required dose reduction or discontinuation of cenobamate.

Conclusions

Cenobamate shows potential benefits in seizure control in patients with SCN2A/SCN8A mutations, although with variable responses, highlighting the need for further studies to confirm these findings.

Genotype-Phenotype Correlation and Epilepsy Treatment in Tuberous Sclerosis Complex: A Sicilian Cohort Study

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Tuberous Sclerosis Complex (TSC) is a rare multisystem disorder frequently associated with early-onset, drug-resistant epilepsy. This retrospective study examined 81 genetically confirmed TSC patients from Sicily (TSC1: 38.3%, TSC2: 61.7%), with a focus on epilepsy phenotypes and genotype correlations.

Patients with pathogenic TSC2 variants demonstrated a significantly higher prevalence of infantile spasms (32% vs. 6.4%, p=0.016), a trend toward more frequent weekly seizures (mean 18.3 vs. 10.4 episodes/week, p=0.089), and more severe structural brain involvement (larger tubers and subependymal nodules, both p0.01). Conversely, TSC1 patients more often presented with radial bands (p=0.011) and a milder neurocognitive profile.

Drug response did not differ significantly between groups, yet seizure remission correlated with better cognitive outcomes: 70% of TSC1 patients and 28.6% of TSC2 patients achieving remission had normal cognitive function. Among drug-resistant cases, severe intellectual disability was noted in 57.1% (TSC1) and 66.6% (TSC2).

EEG analysis revealed more frequent hypsarrhythmia and multifocal abnormalities in TSC2 patients. Antiseizure regimens were heterogeneous: vigabatrin, carbamazepine and valproate and were most used, often in combination with mTOR inhibitors.

This is the first large-scale genotype-phenotype study in Sicilian TSC patients. Our findings reinforce the association between TSC2 variants and more severe epilepsy phenotypes, highlighting the clinical value of early genetic testing. Tailored management strategies - including early mTOR inhibition - may optimize seizure control and cognitive outcomes in high-risk genotypes.

These results support the need for genotype-informed epilepsy care and underscore the relevance of precision medicine in TSC-related epilepsies.

Epilepsy Pharmacotherapy and Outcome Correlates in Pediatric Sturge-Weber Syndrome: A Retrospective Cohort Study

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Background:

Epilepsy is the most disabling manifestation of Sturge-Weber syndrome (SWS) and a major driver of long-term morbidity. Rigorous data on antiepileptic drug (AED) use and effectiveness in this population are scarce.

Methods:

We retrospectively reviewed the medical records of 22 consecutive SWS patients (≤18 y) followed at our tertiary centre between 2002 and 2024. Demographic variables, seizure semiology, neuroimaging, genetics, AED exposure, response (ILAE criteria), and surgical interventions were extracted. Descriptive statistics are reported as median (inter-quartile range, IQR) or n (%).

Results:

Median age at epilepsy onset was 6 months (IQR 3–9); 15/22 (68%) presented within the first year of life. Median follow-up was 10 years (IQR 6–16). Patients trialled a median of 4 AEDs (IQR 3–5). The most frequently prescribed agents were carbamazepine 14/22 (64%), valproate 13/22 (59%), levetiracetam 11/22 (50%), clobazam 9/22 (41%), and topiramate 7/22 (32%). Initial monotherapy achieved ≥12-month seizure freedom in 6/22 (27%). Drug-resistant epilepsy developed in 15/22 (68%), typically after failure of two agents at adequate dose/duration. In this subgroup, rational polytherapy with carbamazepine ± levetiracetam and/or clobazam produced ≥50 % seizure reduction in 4/15 (27%), whereas topiramate and phenobarbital were rarely beneficial. Nine patients underwent epilepsy surgery (disconnective or focal resection); 5/9 (56%) attained Engel I outcome and successfully withdrew ≥1 AED during follow-up. Leptomeningeal involvement and seizure onset

Conclusions:

Early-onset, extensive SWS is strongly associated with AED refractoriness. While initial monotherapy controls seizures in a minority, timely escalation to tailored polytherapy and consideration of surgery can improve seizure control and allow AED burden reduction. Prospective trials are needed to optimise drug combinations in this challenging cohort.

CT perfusion is a valuable tool for the diagnosis of non-convulsive seizures and post-ictal state

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Background:
Non-convulsive seizures (NCS), non-convulsive status epilepticus (NCSE), and post-ictal state (PIS) can mimic acute stroke, posing a diagnostic challenge in emergency settings. Prompt identification improves outcomes. CT perfusion (CTP), commonly used in stroke evaluation, may offer additional value in identifying ictal and post-ictal states. This study aimed to characterize CTP patterns in patients diagnosed with seizures.

Methods:
We retrospectively reviewed medical records of patients who underwent CTP in the emergency room between January 2020 and December 2022 and were diagnosed with a seizure during the same visit. Clinical data, EEG findings, and seizure type (focal or generalized) were recorded. A neuroradiologist reviewed CTP maps (CBF, CBV, MTT, Tmax) for focal hyperperfusion, hypoperfusion, or other distinctive patterns.

Results:
Sixty-nine patients met inclusion criteria; 64 (93%) had focal seizures and 5 (7%) had generalized seizures. Among focal seizure patients, 22% had focal motor symptoms, 36% non-motor, and 35% presented with Todd's palsy. EEG was available in 45 patients, showing epileptic activity in 44%. Abnormal CTP findings were observed in 57 patients (82.6%). In focal seizures, CTP revealed hyperperfusion in 40% and hypoperfusion in another 40%. Among patients with Todd's palsy, 60% showed focal hypoperfusion. Distinctive patterns included occipito-temporal hyperperfusion ("horseshoe" sign) and pulvinar involvement in NCS/NCSE, and focal cortical hyperperfusion surrounding epileptic foci in focal PIS..

Conclusions:
CTP is a valuable, accessible imaging modality for differentiating NCS, NCSE, and PIS from acute stroke in emergency settings.

Evaluation of the effects of antiepileptic therapy on cognitive and psychical functioning and quality of life in school-age children with new-onset epilepsy

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Children with epilepsy face changes in cognitive functioning, the appearance of mental problems, and an unsatisfactory quality of life. As potential causes of these changes, there are factors related to epileptic seizures and side effects of anti-seizure medications (ASMs). However, it is not often possible to draw a clear conclusion when changes occur in the funcioning of children with new-onset epilepsy, i.e., when is the best to react preventively.

A non-interventional, propspective, six-month follow-up study that evaluated the occurrence of internalizing and externalizing symptoms and quality of life in children with newly diagnosed epilepsy was conducted in University children`s hospital in Belgrade. Children and their parents were asked to fill out appropriate questionnaires (i.e., RCADS, NCBRF, CHEQOL-25, KIDSCREEN-10, REVISK and AEP) immediately after the ASM introduction and six months later.

We have shown that there was a significant drop in PIQ after sx months, but ASMs did non influence that decline. Also, RCADS and NCBRF scores were significantly elevated and internalizing and externalizing symptoms influenced each other. ASM significantly influenced the increase of depressive scores of RCADS questionnare, as well as CHEQOL-25 and KIDSCREEN-10 scores.

Adverse effects of ASMs were significantly associated with the manifestation of depressive symptoms and lowering the quality of life. However, they did not significantly affect the decline in cognitive status, the appearance of anxiety, ADHD symptoms, and behavioral disorders.

Keywords: new-onset epilepsy, cognition, behavior, QOL, ASM, adverse effects

Fluoxetine Treatment in Epilepsy of Infancy with Migrating Focal Seizures Due to KCNT1 Variants: An Open Label Study

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Objective

Gain-of-function (GoF) variants in KCNT1 encoding for potassium channels are associated with different epilepsy phenotypes, including epilepsy of infancy with migrating focal seizures (EIMFS), other early infantile developmental and epileptic encephalopathies, and focal epilepsy. Fluoxetine blocks currents from both wild-type (WT) and mutant KCNT1 channels with GoF in vitro features. In this study, we tested the hypothesis that treatment with fluoxetine might improve clinical outcome in patients with EIMFS carrying GoF variants in KCNT1 channels showing in vitro sensitivity to fluoxetine blockade.

Methods

We enrolled three pediatric patients carring de novo KCNT1 genetic variants linked to EIMFS. Functional and pharmacological studies to assess fluoxetine`s ability to counteract in vitro variant-induced functional effects were performed with patch-clamp electrophysiology on heterologous channel expression in mammalian Chinese hamster ovary cells. Neuropsychological assessment, electroencephalogram and seizure diary were evaluated at baseline and every 3 months during the study. Electrocardiography and blood levels of medications were monitored for safety.

Results

All 3 KCNT1 variants displayed GoF effects in vitro. Exposure to fluoxetine (10μM) blocked both WT and mutant KCNT1 channels, therefore, counteracting variant-induced functional effects. Treatment with fluoxetine caused a variable reduction of seizure frequency (25–75%). Improvement in visual attention, participation, and muscle tone was also reported. No adverse events were reported except for transient dyskinesia in 1 patient, which was probably related to an increase in fluoxetine plasma level.

Conclusions

Fluoxetine may be a potential targeted medication in EIMFS caused by KCNT1 GoF variants. Further research is needed to assess its long-term efficacy and safety.

Highly purified cannabidiol (hpCBD) in CDKL5 deficiency disorder (CDD): open label prospective study

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Purpose: CDKL5 deficiency disorder (CDD) is an early-onset developmental epileptic encephalopathy characterized by high seizure burden and drug-resistance, cerebral visual impairment, motor, sleep and gastrointestinal disorders. There is preliminary evidence of highly purified cannabidiol (hpCBD) efficacy in CDD in reducing seizures (Devinsky O. et al. Epilepsy Behav. 2018 Sep;86:131-137) but no reported effects on other comorbidities.
The aim of this study is to further define efficacy and safety of hpCBD in CDD.
Methods: this is a prospective single-center open label study with hpCBD in patients with CDD older than 1 year. We assessed frequency of countable motor seizures, parental and physician perception of global improvement (CGI), changes in sleep, motor performance and EEG at 3, 6 and 12 months after enrollment.
Results: 8/9 patients (9 females, median age 10 years, range 1-24 years) completed the study, one patient withdrew at 6 months due to skin rash. Seizure reduction 50% at 3 months was achieved by 8/9 subjects at 3 months, 7/9 at 6 months, 3/8 at 12 months. In three patients there was a significant improvement in motor performance and in four patients in sleep quality. All caregivers reported at least a minimal global improvement (CGI 3) throughout the study while in three cases there was a great improvement (CGI 2), with a peak at 6 months. At 12 months, all subjects achieved a minimal global improvement, which was the reason for hpCBD continuation despite relative loss of efficacy on seizure frequency. No severe adverse event was recorded during the study.
Conclusions: hpCBD could be a safe and effective option for CDD although efficacy on seizure tends to decrease over time similarly to what happens with most drugs used in this condition. Results suggest a possible global improvement beyond epilepsy. Future trials should include assessment of non-seizure outcomes and compare long-term efficacy of different ASMs.

Seizure control and delivery outcomes in pregnant women with epilepsy.

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Objective: This prospective study aimed to investigate the course of epilepsy during pregnancy, evaluate seizure control in women with focal epilepsy (FE) compared to those with generalized epilepsy (GE), and assess the impact of epilepsy on delivery and neonatal outcomes, comparing adverse outcomes between pregnancies complicated by epilepsy and those without.

Methods: A total of 124 pregnant women with epilepsy (WWE) were enrolled and compared to 277 healthy pregnant women without epilepsy. Obstetric and neonatal outcomes were systematically evaluated.

Results: Seizures during pregnancy were more frequent in women with FE (77.1%) than in those with GE (50.0%) (Odds ratio [OR] 2.08; 95% confidence interval [CI] 0.97–4.46, p = 0.06). Women with GE achieved significantly higher rates of seizure freedom compared to those with FE (p = 0.0038). Poor seizure control was significantly associated with nonadherence to treatment (p0.0001). Compared to healthy controls, WWE had higher risks of cesarean section (p 0.0001) and preterm delivery (p = 0.03). Neonates of WWE also had increased risks of low Apgar scores at 5 minutes (≤7, p 0.0001) and perinatal hypoxia (p=0.03). Seizures during pregnancy were significantly correlated with higher rates of cesarean section, low Apgar scores, and perinatal hypoxia (p = 0.0069, p = 0.0098, and p = 0.0045, respectively). No significant difference in adverse outcomes was observed between FE and GE groups.

Conclusion: Seizures during pregnancy pose significant risks for adverse maternal and neonatal outcomes. Early assessment, effective seizure management before and during pregnancy, and rigorous adherence to treatment are essential to mitigate these risks and improve outcomes for both mother and child.

Fenfluramine in SCN1A-Related GEFS+: A Multicentre Observational Study on Efficacy, EEG Improvement, and Tolerability

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The SCN1A gene is implicated in a broad spectrum of epilepsy phenotypes, ranging from self-limited genetic epilepsy with febrile seizures plus (GEFS+) to severe developmental and epileptic encephalopathies such as Dravet syndrome (DS). While fenfluramine (FFA) has demonstrated strong efficacy in DS, its role in SCN1A-related epilepsies beyond DS has not been thoroughly investigated. We conducted a multicentre observational study including 11 patients with SCN1A-related GEFS+ who received FFA as adjunctive therapy. All patients had previously failed to achieve adequate seizure control with valproate and, in most cases, additional anti-seizure medications. FFA was introduced following the DS titration protocol, with a mean dose of 0.39 mg/kg/day. FFA addition led to a mean seizure frequency reduction of 91%, with more than half of the patients achieving complete seizure freedom. Reduced EEG abnormalities were documented in 6/11 patients of the cohort, including complete normalization in 3/11 patients. Furthermore, subjective caregiver reports indicated perceived improvements in patients' alertness and behavioural responses. FFA was well tolerated, with only mild and transient adverse events reported. These findings support the potential role of FFA as an effective and well-tolerated treatment option in patients with SCN1A-related GEFS+.

Pharmacoresistant Epilepsy in Tuberous Sclerosis Complex (TSC): Clinical Benefit of Combined Everolimus and Purified Cannabidiol Therapy

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Background:
Epilepsy in TSC is frequently drug-resistant, requiring individualized approaches. Everolimus, an mTOR inhibitor, and highly purified cannabidiol (hpCBD) are promising options. We report a case illustrating the benefit of combined therapy.

Case Presentation:
M. is a 7-year-old boy diagnosed with TSC at 2 months following focal seizures in the right hemibody. Brain MRI revealed multiple cortical-subcortical tubers and bilateral subependymal nodules. Despite multiple antiseizure medications (vigabatrin, carbamazepine, levetiracetam, valproic acid), seizure persisted, including daily chin clonus clusters (7–8 events every 10 minutes), and longer episodes with oculomotor deviation and tonic-clonic activity. In 2023, semiology evolved to include behavioral arrest with laughter or shouting. Stereo-EEG identified two epileptogenic foci, but surgery was declined. Everolimus, started at age 3, provided partial benefit but was limited by recurrent infections. In May 2023, hpCBD was introduced, enabling Everolimus dose reduction. This combination led to a marked improvement: ≤1 mild seizure/day, better sleep, and cognitive gains. Vigabatrin was successfully discontinued.

Conclusion:
This case highlights the synergistic potential of Everolimus and hpCBD in managing TSC-related drug-resistant epilepsy. Their pharmacokinetic interaction—raising Everolimus levels—can be advantageous. Combined therapy improved seizure control, neurocognitive function, and treatment flexibility, supporting its use in similar cases.

Long-term open-Label study evaluating oral Miglustat treatment in patients with Neuronal Ceroid Lipofuscinosis Type 3

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Objective: Neuronal ceroid lipofuscinosis type 3 (CLN3) is a rare lysosomal storage disorder characterized by progressive neurodegeneration. No disease-modifying treatments are currently available. Miglustat, a substrate reduction therapy, has shown preclinical efficacy in CLN3 models. This study aimed to assess the long-term safety and clinical impact of miglustat in patients with CLN3 disease.

Methods: This was an open-label, single-center study conducted at Bambino Gesù Children's Hospital in Rome, Italy. Oral miglustat was titrated to 15 mg/kg/day or a maximum of 600 mg/day. Patients were assessed every six months using the Unified Batten Disease Rating Scale (UBDRS). The primary outcome was the annual rate of change in the UBDRS physical subscale. Clinical data were analyzed descriptively.

Results: Six patients (33% female) with a median age of 20.34 years (IQR: 18.25 - 23.84) were treated and followed for a median of 3.9 years (IQR: 3.32 - 4.34). The mean annual change in UBDRS physical score was +0.16 points/year (SD ±1.48). Miglustat was well tolerated, with only mild, self-limiting gastrointestinal side effects observed.

Discussion: Miglustat showed a favorable safety profile and was associated with a slower rate of physical decline compared to historical controls. Limitations include small sample size, genetic heterogeneity, and open-label design.

Attitude of people with epilepsy in Serbia towards surgical treatment of epilepsy

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Objective: One-third of patients with epilepsy (PWE) have drug-resistant epilepsy (DRE), which leads to various negative socioeconomic consequences and increases the risk of sudden unexpected death in epilepsy (SUDEP). Surgical treatment is considered the most effective option for patients with lesional DRE. We aimed to assess the awareness and attitudes of PWE in Serbia toward epilepsy surgery (ES).

Methods: This multicenter study included 247 consecutive PWE referred to various centers in Serbia between May 2023 and September 2024. Participants voluntarily completed a self-reported 27-item questionnaire, covering socioepidemiological data, patients' epilepsy, any previous surgery, awareness of epilepsy treatment modalities, with last six questions in form of hypothetical scenarios, in which patients had to choose whether to accept or refuse ES when faced with its different estimated efficacy and risk.

Results: Less than half of the participants were familiar with ES. Only 16.6% of the patients expressed willingness to undergo ES when presented as a safe and effective therapeutic option. Patients without adequate seizure control, with history of ictal injuries and hospitalization due to seizures were more motivated for ES. The most common reasons for accepting surgery were the potential for freedom from ASMs and improved seizure control. The most frequent reasons for rejecting it were perception of adequate seizure control with ASMs and fear of surgery complications.

Conclusion: PWE in Serbia are not adequately informed about the epilepsy surgery. A multidisciplinary approach, combined with greater media involvement, is essential to raise awareness about this effective treatment option for those with DRE.

Quantitative EEG Biomarkers of Long-Term Response to Lacosamide in Drug-Naive Focal Epilepsy

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Purpose: Lacosamide (LCM) is an antiseizure medication approved for focal-onset seizures, however its effects on cortical activity and connectivity remain unclear. This study investigated quantitative EEG (qEEG) changes induced by LCM monotherapy in drug-naive adult people with epilepsy (PwE) compared to healthy controls (HC), and explored the predictive value of qEEG for long-term seizure outcomes. Methods: We conducted a retrospective, longitudinal pharmaco-EEG study on 20 PwE and 24 HC. PwE were evaluated two years after LCM initiation and classified as seizure-free (SF) and non seizure-free (NSF). Resting-state EEGs were recorded before (30 days) and 6 months after LCM initiation. Power Spectral Density (PSD) and Amplitude Envelope Correlation (AEC) were computed across five frequency bands (delta, theta, alpha, beta, gamma), using 19-channel EEG processed with Brainstorm software. Wilcoxon tests compared PSD and AEC between Condition (pre-LCM, post-LCM, HC) for each frequency band and logistic regression assessed the performance of qEEG in predicting clinical outcome. Results: No significant qEEG changes were observed between pre- and post-LCM. Theta-band PSD and connectivity were higher in PwE than HC, both pre (connectivity, $p = 0.038$; PSD, $p = 0.04$) and post LCM (connectivity, $p = 0.007$; PSD, $p = 0.005$). AEC connectivity in the theta band predicted 2-years seizure freedom with an accuracy of 60% (area under the curve [AUC] = 0.66) for the EEG pre-LCM and 75% (AUC = 0.86) for the EEG post-LCM. Conclusions: These findings support the use of pharmaco-EEG as a non-invasive tool for predicting long-term clinical outcomes in focal epilepsy.

Fenfluramine treatment in children with Dravet syndrome: A retrospective and observational audit.

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Background: Dravet syndrome is a lifelong, severe, drug resistant developmental and epileptic encephalopathy (DEE) with infantile onset epilepsy associated with recurrent prolonged seizures and intellectual disability. Fenfluramine is now licensed for use in Dravet syndrome as add on therapy. We aim to describe the efficacy and tolerability of fenfluramine in children with Dravet syndrome.
Methods: A retrospective observational study at Great Ormond Street Hospital, London, England. 33 children with Dravet syndrome with pathogenic SCN1A variant were enrolled who were treated with fenfluramine between 2019 to 2025 and followed up for at least one year.
Results: Thirty- three children (15 Male) were included. Mean age at seizure onset and diagnosis were at 6 months and 24 months respectively. Fenfluramine was started at median age of 9.35 years (range 2.5 years-19 years) with mean maintenance dose of 0.34 mg/kg/day (range 0.12 mg/kg/day – 0.71 mg/kg/day). Eight (24.24%) children discontinued treatment due to lack of efficacy or adverse effects.
At last follow up, generalized tonic-clonic seizures were reduced by ≥75% in 10 (50%) children, 50% -75% in 4 (20%) children, by 30%-50% in 4 (20 %) children and by 30% in 2 (10%) children. Additionally, at least one medication was weaned off in 8 (30.30%) children. Loss of appetite 11 (33.33%) was the commonest side effects followed by worsening of seizure (15.15%), tiredness (12.12%), worsening behaviour (12.12%), volatile mood/low mood (9.09%). No abnormalities detected in echocardiography during the treatment period.
Conclusion: Fenfluramine resulted in significant reduction in seizure frequency and also reduction in concomitant antiseizure medication in children with Dravet syndrome.

Predictors of new-onset seizures following stereotactic radiosurgery for brain metastases

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Introduction
Stereotactic radiosurgery (SRS) has revolutionized the treatment of metastatic brain tumors. Despite its effectiveness, SRS can lead to side effects, including new-onset seizures. Although a rare complication, seizures could increase morbidity and impact overall quality of life. Identifying factors associated with seizure onset post-SRS is crucial to improve patient care and optimize treatment.
Materials and Methods
A retrospective observational study included patients treated for brain metastases at our tertiary center over a five-month period. Data on demographics, primary malignancy, disease course, previous treatment, and SRS intervention were collected. Patients with a prior history of seizures were excluded.
Results
The study cohort consisted of 101 patients, of whom 9 (8.9%) developed seizures post-SRS, with a median time to seizure onset of 8.2 months. Patients with seizures had higher functional disability at admission (ECOG-PS score: 2 (0-3) vs. 1 (0-3), p=0.02), and focal neurological deficit was more frequent (77.8 vs. 52.2%, p=0.03). The frequency of previous extracranial radiotherapy and immunotherapy was also higher in this group (p=0.04, p=0.05). A greater total number of SRS interventions correlated with seizure onset (2 (1-3) vs. 1 (1-5), p=0.001), as well as midline shift on preprocedural brain MRI (p=0.01) and metastatic disease progression on follow-up MRI (p=0.01). In bivariate logistic regression, higher ECOG-PS scores and midline shifts were independent predictors of seizure onset.
Conclusion
Our results suggest that patients with higher functional disability measured by ECOG-PS score and midline shifts on preprocedural brain MRI are at increased risk of new-onset seizures following SRS.

Quantitative EEG analysis of brivaracetam in drug-resistant epilepsy: A pharmaco-EEG study

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Objective: Brivaracetam (BRV) is an antiseizure medication (ASM) approved as add-on therapy for people with focal epilepsy. BRV has good efficacy and safety profile compared to other ASMs. However, its specific effects on resting-state EEG activity and connectivity are unknown. The aim of this study is to evaluate quantitative EEG changes induced by BRV therapy in a population of adult people with drug-resistant epilepsy (PwE) compared to healthy controls (HC).

Methods: We performed a longitudinal, retrospective, pharmaco-EEG study on a population of 23 PwE and a group of 25 HC. Clinical outcome was dichotomized into drug-responders (i.e., 50% reduction in seizures` frequency; RES) and non-responders (N-RES) after two years of BRV. EEG parameters were compared between PwE and HC at baseline (pre-BRV) and after three months of BRV therapy (post-BRV). We investigated BRV-related variations in EEG connectivity using the phase locking value (PLV).

Results: BRV therapy did not induce modifications in power spectrum density across different frequency bands. PwE presented lower PLV connectivity values compared to HC in all frequency bands. RES exhibited lower theta PLV connectivity compared to HC before initiating BRV and experienced an increase after BRV, eliminating the significant difference from HC.

Conclusions: This study shows that BRV does not alter the EEG power spectrum in PwE, supporting its favourable neuropsychiatric side-effect profile, and induces the disappearance of EEG connectivity differences between PwE and HC.

Significance: The integration of EEG quantitative analysis in epilepsy can provide insights into efficacy, mechanism of action, and side effects of ASMs.

Epidyolex® in Lennox Gastaut, Dravet Syndrome and Tuberous Sclerosis Complex: an observational study in Italy

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Background: Epidyolex® (highly purified cannabidiol, hpCBD) has been approved as adjunctive therapy for seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS) and Tuberous Sclerosis Complex (TSC) in patients aged ≥2 years. These rare developmental and epileptic encephalopathies are characterized by pharmacoresistant seizures, profound neurological dysfunction, and significant cognitive and behavioral comorbidities. While randomized controlled trials (RCTs) have established the efficacy and safety profile of hpCBD, their generalizability is limited by highly selective study populations. Consequently, real-world evidence (RWE) is essential to evaluate therapeutic outcomes in more heterogeneous, clinically representative cohorts.

Methods: This prospective, multicenter, observational study will enroll approximately 70–100 pediatric and adult patients diagnosed with LGS, DS, or TSC who are prescribed hpCBD within routine clinical practice in Italy. The primary endpoint is treatment retention at Weeks 4, 16, 28, 40, and 52, serving as a pragmatic surrogate for long-term clinical effectiveness. Secondary endpoints include seizure frequency, titration patterns and maintenance dosages, adverse events (AEs) incidence, and changes in quality of life (QoL), behavior (Child Behavior Checklist, CBCL), and non-seizure-related outcomes (NSROs). Exploratory endpoints include responder rates (≥25%, ≥50%, ≥75% seizure reduction) and seizure-free days.

Discussion: Reflecting routine medical practice, this study will generate RWE on the long-term use of hpCBD, capturing data on effectiveness, safety, and broader patient-centered outcomes including cognitive and behavioral functioning.

Conclusion: The study will provide clinically relevant RWE regarding the long-term safety, effectiveness, and functional impact of hpCBD in LGS, DS, and TSC, informing evidence-based treatment strategies in routine care settings.

Efficacy and tolerability of Cenobamate: real-world experience from an Italian tertiary Center.

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Objective: To investigate the real-world efficacy and tolerability of cenobamate (CNB) in persons with drug-resistant epilepsy (DRE) attending an Italian tertiary epilepsy center.

Method: This single-center, retrospective observational study was conducted at Bellaria Hospital between 2022 and 2025. The inclusion criteria were age≥ 18 years, focal DRE, and follow-up durationf≥6 months. Data were extracted from medical records. Primary endpoints included seizure reduction rates (≥50-80%, ≥80.1-99%, 100%), adverse events (AEs), retention rates and average dose of CNB at 3, 6 and 12 months.

Results: We included 98 people with DRE. Etiology was known in 71.4% of cases (68.5% structural, 20% genetic, 7.2% autoimmune, 4.3% post-infectious). At baseline, median duration of epilepsy was 26 years, with a median of 12.3 seizures/month. The median number of previous and concomitant antiseizure medications (ASMs) was 6 and 3, respectively. Retention rates at 3, 6 and 12 months were 99%, 91.6% and 83.7% with corresponding mean CBN doses of 112 mg, 148 mg and 179 mg/day. At the final follow-up, seizure freedom was achieved in 21.9% of patients; 28.7% and 17.8% achieved ≥50–80% and ≥80.1–99% seizure reduction, respectively. A significant reduction in seizure frequency was observed at all time points (P 0.001). The cumulative incidence of AEs was 46.9%, 44.3%, and 44.8% at 3, 6, and 12 months, respectively.

Conclusions: CNB demonstrated favorable efficacy in individuals with DRE of diverse etiologies, even at doses 200 mg/day. Although AEs were frequent, they did not significantly impact retention, which remained high throughout the study period.

State-Of-The-Art Of The Gaba-Pathies Current Treatment

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This study investigates treatment outcomes and medication efficacy in a cohort of individuals with genetic epilepsies secondary to GABAA receptor variants. After functional characterization, individuals were categorized by gain-of-function (GoF) and loss-of-function (LoF) mutations. A total of 80 patients were surveyed. LoF patients demonstrated a higher likelihood of seizure control across treatment lines than GoF patients.

Medication-specific trends revealed that LoF individuals responded better to valproate (VPA), clobazam (CLB), and carbamazepine (CBZ), while GoF individuals showed improved outcomes with cannabidiol (CBD) and lacosamide (LCM). Perceived efficacy and seizure freedom rates varied significantly between groups, with LoF patients generally reporting better outcomes. Adverse effects were common, particularly with sodium channel blockers and benzodiazepines, and varied by mutation type.

Non-pharmacological interventions such as the ketogenic diet and vagus nerve stimulation (VNS) were trialed in select cases, with mixed results. The ketogenic diet showed moderate efficacy, particularly in GoF patients, while VNS had limited success.

This analysis highlights the importance of genotype-specific treatment strategies in epilepsy management. The findings support a more personalized approach to ASM selection and underscore the need for early, targeted interventions to maximize seizure control and minimize adverse effects.

Depression in people on Anti-Seizure Drug (ASD) Therapy

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Purpose: Depression is one of the most common comorbidities in people with epilepsy due to neurobiological and psychosocial reasons. Some old and new ASDs are also considered to be risk factors of depression, although the causes for these phenomena are not fully understood. The Aim of our study was to disclose depression cases in people treated with varios type of ASDs.

Methods:The study was performed using Beck`s Depression Inventory (BDI) among eighty patients with epilepsy (aged 18-65 years) on ASD treatment more than six mouths with CBZ-13 (MD=700 mg/day), VPA-10 (1000 mg/day), LEV-21(MD=1250 mg/day), LTG-13 (MD=150 mg/day), and polytherapy-23, mostly with CBZ (MD=700 mg/day) and LEV (MD=1500 mg/day).The presence and severity of depression were assessed according BDI scores as follows:No depression (1-10), Mild mood disturbance (11-16), Borderline clinical depression (17-20), Moderate depression (21-30), Severe depression (31-40), Extreme depression (40).

Results:Out of 80 patients 40 (50%) revealed different degrees of depression: 24 (30%) mild, 9 (11%) borderline, 4 (5%) moderate and 3 patients (4%) severe depression was disclosed. Depression was most frequent in patients on Polytherapy (70%) and most rare-on LTG (38%) and low doses of LEV (38%).

Conclusion:The risk of depression is higt in patients on polytherapy, which requiers more attention for prevention of depression in cases of polytherapy.

Note:The study was performed in a frame of CIU-grant (NºCIU-FR-125-22).

Efficacy and side effects of fenfluramine treatment in children with Dravet syndrome and Lennox-Gastaut epileptic encephalopathies in Israel

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Introduction:

Children with Dravet syndrome, Lennox-Gastaut syndrome, and other epileptic encephalopathies often require multiple treatment lines to manage seizures effectively. Fenfluramine was recently approved for seizure treatment in children aged two years and older with Dravet and Lennox-Gastaut syndromes. This study aims to assess the efficacy of fenfluramine and the incidence of side effects in children with these syndromes in Israel.

Methods:

This retrospective multicenter study involved five medical centers across Israel. Patients treated with fenfluramine for at least three months were included. Data collected comprised demographics, clinical diagnosis, seizure frequency, concomitant antiepileptic medications, fenfluramine dosage, treatment response, and adverse effects.

Results:

Seventy-one patients were included, with 56% diagnosed with Dravet syndrome, 29% with Lennox-Gastaut syndrome, and 12% with other epileptic encephalopathies. The average treatment duration was 11.9 months, and the mean age was 10 years. Moderate to severe developmental delay was observed in 66% of patients, and 60% had communication disorders. Treatment response was seen in 46% of patients, with the highest response rate (66%) among those with Dravet syndrome. Responders were more likely to have moderate to severe developmental delay ($p=0.04$), concurrent clobazam treatment ($p=0.035$), and higher trough valproic acid levels ($p=0.05$). Side effects were reported in 22 patients, most commonly fatigue (45%). One patient developed new valvular heart insufficiency.

Discussion:

Fenfluramine is a valuable treatment option for epileptic encephalopathies, particularly effective in Dravet syndrome. The main side effects observed were fatigue and decreased appetite; however, monitoring of cardiac valvular structure is necessary.

Quantitative Hippocampal and Amygdalar Volumetry in Epileptic Patients Using SWANe Post-Processing

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Objectives: To quantitatively assess hippocampal volume in focal and generalized epilepsy using high-resolution 3T MRI processed via the SWANe post-processing pipeline.

Materials and Methods: MRI data acquired at our center using a 3T scanner and HARNESS protocol (3D T1-weighted and 3D FLAIR) were retrospectively analyzed in 43 patients with focal or generalized epilepsy. Clinical and EEG data were collected from medical records. SWANe software, incorporating FreeSurfer-based segmentation, was used to extract hippocampal and amygdalar volumes. Volumes were normalized using z-scores based on a normative database. Interhemispheric asymmetry was also evaluated. Imaging findings were integrated with clinical and EEG data.

Results: In focal epilepsy with known lateralization (n = 31), hippocampal atrophy concordant with the presumed epileptogenic hemisphere was identified in 58.1% of patients (mean z-score difference: −0.84). In temporal lobe epilepsy (n = 20), concordance was 50% (mean difference: −0.95). Severe hippocampal atrophy (z-score −2) was found in 12.9% (n = 4). Notably, hippocampal atrophy (z-score −1.5) was detected in 10 patients whose MRIs had no reported abnormalities. Amygdala volumetry did not show consistent lateralization, with hemispheric concordance of 48.4% in focal epilepsy and 45% in TLE. Mean z-score asymmetries were −0.11 and −0.26, respectively. Only 3 patients had clearly abnormal amygdalar volumes (z-score −2). In generalized epilepsy, no relevant asymmetries or focal atrophy were observed, consistent with diffuse seizure activity.

Conclusion: SWANe enables objective quantification of hippocampal volume, improving detection of subtle abnormalities missed by routine MRI. Comparison with normative data may refine epileptogenic zone identification and support clinical decision-making.

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The role of ASMs in patients with cognitive deficits and EEG changes along the epileptic-encephalopathic continuum

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Introduction
Young patients with cognitive changes require a broad differential diagnosis. Interictal epileptiform discharges and non-specific EEG changes along the epileptiform-encephalopathic continuum, without clear seizures, is often difficult to interpret. We present four patients with ASM-responsive cognitive changes, who do not meet the clinical criteria of epilepsy.
Cases
A 54 YOF with headache and intermittent confusion, normal MRI, lumbar puncture, and autoimmune serology, had intermittent bilateral temporal slowing and occasional temporal sharp waves on video-EEG monitoring. Cognitive improvement followed lamotrigine treatment.
A 19 YOF with epilepsy family history and syncope events had diffuse slowing and temporal epileptiform discharges on EEG and was given lamotrigine. She felt more focused but stopped treatment due to headache and dizziness. This was followed by cognitive worsening and lamotrigine reintroduction resulting in improved attention.
A 14 YOF developed new-onset MOGAD-induced non-convulsive status epilepticus (NCSE) and was successfully treated with immunomodulation and ASMs. Following ASMs discontinuation, she had fluctuating attention deficit, runs of theta slowing and occipital sharp waves on EEG, and oxcarbazepine, subsequently switched to lamotrigine, resulted in clinical improvement.
A 30 YOF treated with CAR-T for lymphoma, had myoclonus, tonic-clonic seizures, and NCSE, as part of ICANS. Following withdrawal of ASMs, she had confusion and diffuse theta slowing. Attempts to decrease lacosamide resulted in cognitive worsening. She switched to lamotrigine, with stable cognitive function.
Conclusion
These cases underscore the utility of EEG in evaluating cognitive complaints and support a therapeutic trial of ASMs in selected patients with overt albeit nonspecific EEG abnormalities.

Effectiveness Of Epidiolex And Whole-Plant Medical Cannabis For Seizure Control In Tuberous Sclerosis Complex: Real-World Clinical Experience

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Tuberous sclerosis complex (TSC) is a rare genetic disorder frequently associated with treatment-resistant epilepsy. Epidiolex (purified cannabidiol, CBD) is FDA-approved for seizure control in TSC, but real-world data on the efficacy of whole-plant medical cannabis remain limited.

A retrospective observational study was conducted in 41 patients with TSC-associated epilepsy (mean age 30.5 years). Patients were divided into three treatment groups: Epidiolex (n=7), whole-plant medical cannabis (n=3), and standard anti-seizure medications without cannabinoids (n=31). Outcomes over six months included seizure frequency, treatment tolerability, and patient-reported quality of life. A ≥50% reduction in seizure frequency was defined as a clinically meaningful response.

At six months, 71.4% of Epidiolex users (5/7) experienced significant seizure reduction, with most reporting better quality of life and good tolerability. In the whole-plant cannabis group, 33.3% (1/3) had partial seizure reduction, though the small sample size limits interpretation. Only 16.1% (5/31) of patients on standard medications achieved similar improvement, with many reporting side effects like fatigue and cognitive issues.

Although logistic regression showed a non-significant trend favoring Epidiolex (OR=5.2; p=0.06), the small sample limited statistical power.

Conclusions:

In this real-world cohort of patients with TSC, Epidiolex was associated with greater seizure reduction and improved tolerability compared to whole-plant medical cannabis or standard anti-seizure medications. While the findings are promising, limitations include small sample sizes and a retrospective design. Further prospective, controlled studies are warranted to clarify the role of both purified and whole-plant cannabinoids in the management of TSC-related epilepsy.

Efficacy and tolerability data of cannabidiol use in a population of adult patients with Lennox-Gastaut syndrome

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Rationale and Objectives

Cannabidiol (CBD) is approved in Italy as an add-on treatment for patients with Dravet syndrome, Lennox-Gastaut syndrome (LGS), and Tuberous Sclerosis Complex (TSC). However, data on efficacy and tolerability in adult patients remain limited to date.

Methods

Clinical and instrumental data were prospectively collected from adult patients with LGS undergoing treatment with CBD, followed at the Epilepsy Centers of the San Martino Policlinic Hospital (Genoa) and the Civil Hospital of Baggiovara (Modena) from September 2021 to January 2024. Data on efficacy and tolerability were then analyzed.

Results

Eighteen patients were recruited (age range 18–51 years, median age 26.5), of whom 50% were female. The baseline monthly seizure frequency was 75.8 ± 93.5 (range 12–430), and the frequency of drop seizures, present in 15/18 patients, was 7.9 ± 13.9 (range 1–60). At 6- and 12-month follow-ups, the retention rates were 100% and 92.9%, respectively. Responders accounted for 50% at 6 months and 35.7% at 12 months, with a greater reduction in drop seizures and seizure clusters. No severe adverse reactions were reported. Eleven patients experienced at least one adverse effect, which was mild in 71% of cases.

Conclusions

Treatment with CBD in adult patients with LGS proved effective in significantly reducing drop seizures and clusters, with a good tolerability profile.

A prick is enough! Therapeutic drug monitoring of antiseizure medication through capillary microsampling devices

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Background: Capillary blood sampling with microsampling devices, such as Volumetric Absorptive Microsampling (VAMS) and quantitative Dried Blood Spot (qDBS), offers a less invasive alternative for therapeutic drug monitoring (TDM) in persons with epilepsy (PwE). This study evaluated the real-life feasibility, reliability, and analytical performance of at-home blood collection using VAMS devices shipped by regular mail for antiseizure medication (ASM) quantification.

Methods: Carbamazepine, lacosamide, lamotrigine, and levetiracetam concentrations were analyzed through a validated UHPLC-MS/MS method. At-home reliability was assessed by comparing ASM concentrations from self-collected capillary VAMS samples obtained at home versus an ambulatory setting. Feasibility was evaluated through the rate of successfully returned devices and a patient survey addressing ease of use and pain perception. qDBS performance was assessed by comparing ASM concentrations with those from venous plasma and ambulatory VAMS. Agreement between matrices was evaluated using Bland-Altman analysis and Passing-Bablok regression.

Results: Among 103 PwE (66% female, age 19-87 years), 87 sampling kits were successfully returned, and 81 surveys analyzed. Most PwE found the procedure easy (90.12% rated 1/5 for difficulty) with minimal discomfort. qDBS samples showed good quality, with 37.5% achieving a perfect score. Analytical results demonstrated good agreement between microsampling devices and plasma for all ASMs, confirmed by Bland-Altman and Passing-Bablok analysis.

Conclusions: Home-based capillary blood sampling using VAMS and qDBS devices is a feasible, reliable, and well-accepted strategy for TDM in PwE, supporting decentralized TDM and enhancing telemedicine-based care.

Epilepsy Evolution in Patients Following Surgical Intervention: A Clinical-Neurological Perspective

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This study analyzed the long-term clinical and neurological outcomes of 64 patients (aged 17–66 years) who underwent surgical treatment for epilepsy. The cohort included individuals with structural epilepsy (93.8%) and epilepsy of unknown etiology (6.25%), observed over a post-surgical period of 3–5 years. All participants underwent comprehensive clinical, neurological, and neuropsychological assessments. Etiological classification was performed according to the ILAE 2017 framework, with key distinctions from previous classifications outlined.

Effective invasive treatment was achieved in 87.5% of patients. Favorable prognostic outcomes were most notable in individuals with a duration of conservative therapy under five years, where 90% experienced a reduction in seizure frequency by over 50% following surgery. In 90.7% of cases, there was a marked decrease in seizure frequency and duration, reduced tendency toward seizure clustering, and a shift in seizure type — all contributing to improved clinical trajectories and reduced progression of cognitive, focal, and behavioral complications.

Nevertheless, 81.25% of patients developed postoperative complications. These included memory impairment (42.3%), hemiparesis (38.5%), dysphasia (19.2%), and hemorrhagic events (7.7%). The effectiveness of surgical intervention was strongly influenced by seizure type classification, pharmacoresistance status, epilepsy etiology (ILAE 2017), and the duration of conservative treatment prior to surgery.

Despite the overall success of surgical therapy, certain pharmacoresistant forms of epilepsy remain incurable, underscoring the need for further refinement of diagnostic algorithms and individualized treatment approaches.

The significance of Electroencephalography in patients with Epilepsy with Eyelid Myoclonia or Jeavon Syndrome – Case report

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Epilepsy with eyelid myoclonia or Jeavon syndrome is an idiopathic generalized epilepsy characterized by a triad of: eyelid myoclonia with or without absence seizures, EEG paroxysms caused by eyelid closure (epileptiform outbursts bilaterally consisting of spike-wave complexes of 3 Hz) and photosensitivity. The onset occurs in childhood with a peak age of 6-8 years. The overall prognosis of the disease is good, although in this type of epilepsy the treatment is lifelong. Many patients develop medically refractory epilepsy while seizures tend to persist throughout life. Jeavon syndrome is a type of reflex epilepsy. There is a female predominance over the male gender. Intellectual disability and psychiatric disorders are not rare. There are focal EEG abnormalities that are frequently observed and present in two-thirds of cases. A good knowledge of the clinical characteristics allows a quick diagnosis and the start of treatment in these patients. However, this syndrome is often under-reported and under-recognized by medical personnel. Treatment should be aimed at controlling seizures. Antiepileptic choices include Levetiracetam, Sodium Valproate, Lamotrigine, and Ethosuximide, although drug resistance is not uncommon. It has also been shown to respond favorably to the ketogenic diet. Therefore, a good knowledge of the syndrome and a high level of suspicion for it with the help of diagnostic methods (EEG, MRI) are needed to establish an accurate diagnosis. A routine EEG is sufficient to diagnose Jeavon syndrome (multiple spikes and slow waves with a frequency of 3-6 Hz).

Keywords

Epilepsy with eyelid myoclonia, Jeavon syndrome.

Personalized management of severe nonketotic hyperglycinemia

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1. Case Presentation: A 2-year-old girl presented with refractory tonic-clonic seizures starting in infancy, progressing to coma (GCS 3) despite multiple antiseizure medications (ASMs), developmental delay/ Hereditary history was unremarkable.

2. Diagnostic Breakthrough: Biochemical screening revealed significantly elevated plasma glycine (906.9 μM/L) and HPLC amino acids in urine glycine (2120 μM/M).

WGS confirmed the diagnosis: AMT-associated Neonatal Nonketotic Hyperglycinemia.

3. Personalized Therapeutic Strategy:

o Pathogenic therapy: Sodium benzoate (well-tolerated). Dextromethorphan (5mg/kg) caused transient lethargy.

o Protein-restricted diet.

o Critical step: Discontinuation of contraindicated ASMs.

o Continued tailored ASM selection.

4. Challenges & Adaptation: High sensitivity to triggers (teething, infections) caused seizure exacerbations requiring prolonged hospitalization. Persistent seizures prompted initiation of the ketogenic diet.

5. Treatment Outcomes: Gradual reduction in plasma glycine and significant decrease in seizure frequency was achieved, enabling outpatient management under multidisciplinary team supervision.

6. Key Conclusions:

o Genetic diagnostics is crucial for definitive diagnosis of rare disorders like NKH, allowing for personalized, pathophysiology-driven treatment (e.g., sodium benzoate, specific ASM avoidance).

o The ketogenic diet is a potent therapeutic option for achieving seizure control in NKH when standard ASMs and glycine-reduction therapy prove insufficient or response is unstable.

o Effective management of complex orphan diseases like NKH necessitates close collaboration within a multidisciplinary team (genetics, neurology, nutrition, intensive care) for comprehensive care and adapting therapy to dynamic clinical challenges.

Influence of sex hormones on the course of the disease in young men with epilepsy

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Hormonal changes in sex hormones in men have hardly been studied, despite the possible significant impact of epilepsy on the hormonal spectrum in general and on sex hormones in particular, and hormonal dysfunction is also a known factor in the worsening of the clinical course of epilepsy. The aim of this study was to investigate sex hormones in young men with epilepsy depending on the age of epilepsy onset, clinical course of the disease, type of seizures and form of epilepsy. General trends were found in all patients with epilepsy: increased estradiol, decreased prolactin, and decreased testosterone. The degree of hormonal imbalance in patients with epilepsy depended on the age of epilepsy debut (prepuberty, puberty, post-puberty), the type of seizures and the clinical course of epilepsy. On the one hand, hormonal imbalance of sex hormones is one of the factors that reduce the quality of life, and on the other hand, it can be one of the mechanisms of formation of a self-sustaining epileptic system.

The comorbidity between migraine and epilepsy in young men

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It is known that patients with epilepsy are 2-5 times more likely to have comorbid disorders such as migraine. Epilepsy and migraine are common chronic neurological disorders presenting with paroxysmal attacks of transient cerebral dysfunction, followed by subsequent return to baseline between episodes. The migraine aura-triggered seizures are not the only option for combining migraine and epilepsy. The postictal headache and hemicrania epileptica are also isolated according to ICHD-III. The purpose of this study is to establish the relationship between headache and epilepsy in young men. The study were conducted on the basis of the analysis of
clinical symptoms and instrumental methods. EEG, EEG-video monitoring and MRI were used as the screening methods. The intensity of headache was assessed using a visual analogue scale (VAS). Analysis of the data of 80 patients showed that the migraine auratriggered seizures were observed in 28 men (35%), hemicrania epileptica in 22 (27.5%) and postictal headache in 30 patients (37.5%). In the first type, the EEG recorded spike-slow-wave complexes mainly in the left temporal leads, in the second - bilateral continuous spike-and-slow-wave discharges, and in the third - high voltage theta activity intermingled with sharp waves over occipital region.
The brain MRI showed secondary brain lesions in the temporo-parieto-occipital region with a restricted diffusion in the occipital region or enlarged sulci in the parietal region. The comorbidity of migraine and epilepsy has been known for more than a century. Migraine and epilepsy are both complex brain diseases that cause periodic seizures and impair the performance. However, these conditions require further study in young men with epilepsy.

Trends in utilization of cannabidiol (Epidyolex) in severe epilepsies in Norway

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Background: Cannabidiol (Epidyolex) is approved as add-on treatment in Dravet and Lennox Gastaut syndrome and epilepsy in tuberous sclerosis complex since 2019, and formal approval for reimbursement from 2022 in Norway. The extent of its use is still not elucidated.

Purpose: The aim of the present study was to investigate how the prescriptions and use of cannabidiol (Epidyolex) changed since its approval in Norway.

Methods: The Norwegian Prescription Database and Medicines Registry available from the National institute of public health in Norway was used (2020-2024), as a follow-up from our previous pharmacoepidemiological studies.

Results: The number of users was rather stable since approval; 118 in 2020 to 113 in 2024, but with a peak of 179 users in 2023. There was a small predominance of female users overall, although men accounted for 51% in 2021 and 2024. The largest age group in 2020 was 50-54 years (13%), shifting to 25-29 years in 2024 (14%). Notably, users aged ≤ 19 increased markedly from 0 in 2020 to 34.5% in 2024. The total defined daily doses (DDDs) also increased accordingly from 764 to 20804 (2020-2024). Furthermore, clinical use of cannabidiol in patients followed at the National center for epilepsy will be further evaluated regarding pharmacokinetic variability and interactions.

Conclusion: The present results elucidate a limited and stable use of cannabidiol in Norway since its approval. The use of prescription data contributes to focus on drug surveillance in vulnerable patient groups on a national scale.

Effect of Cenobamate on EEG Functional Connectivity in Drug-Resistant Focal Epilepsy: A Pilot Study with High-Density EEG

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Objectives: To assess the effects of cenobamate (CNB) on functional brain connectivity in focal drug-resistant epilepsy (DRE) using high-density EEG (HD-EEG), and to explore network parameter differences between treatment responders and non-responders.

Materials and Methods: Six adult patients with focal DRE were enrolled at the University Hospital of Cagliari. All underwent resting-state 64-channel HD-EEG before and one year after initiating 200 mg/day CNB. From each recording, twenty artifact-free 4-second epochs were filtered into five frequency bands. Phase Lag Index (PLI), weighted clustering coefficient (Cw), and characteristic path length (Lw) were computed via BrainWave software. Paired t-tests assessed differences. Responders were defined by ≥50% seizure reduction based on diaries.

Results: Three patients were responders (two became seizure-free). No significant changes were found in PLI, Cw, or Lw across the full group. In responders, a non-significant trend toward increased Lw in the alpha band was noted ($p = 0.0729$). Only mild, reversible side effects were reported.

Discussion: Although not statistically significant, the trend toward increased Lw in responders may reflect a partial desynchronization effect of CNB on cortical networks. No similar trends were seen in non-responders. These findings align with clinical improvements and reduced epileptiform activity observed in visual EEG analysis. HD-EEG allows detailed functional connectivity analysis by combining high temporal and spatial resolution.

Conclusions: CNB may modulate cortical networks in DRE, particularly in responders. Despite limited sample size, observed trends support further research in larger cohorts. Integration with imaging-based connectomics may enhance insights into CNB's neuromodulatory action.

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Effect of antiseizure medications (ASMs) on bone mineral density in young men with epilepsy

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ASMs had an adverse effect on bone tissue, increasing the risk of fractures in patients with epilepsy. In young men, bone tissue is actively forming, and the negative effects of ASMs may be more pronounced, especially with long-term use.

The purpose of this study was to investigate mineral metabolism and bone mineral density in young men with epilepsy. The study involved 45 men aged 18 to 44. Participants were divided into 3 groups depending on the drug used. Group 1 included 15 men who took first-generation ASMs (phenobarbital). Group 2 included 14 people who took second-generation ASMs (carbamazepine). Group 3 included 16 young men who took third-generation ASMs (levetiracetam). The median duration of ASMs use was 7 (3–14) years. A comparative analysis of laboratory parameters of trace elements and hormones associated with bone metabolism revealed statistically significant differences in the mean values of calcium, phosphorus, parathyroid hormone, and vitamin D. Vitamin D levels in patients in groups 1 and 2 were lower than in group 3 ($p (U) = 0.05$). However, in all three groups, vitamin D levels were insufficient compared to the control group ($p (U) = 0.01$). The Ca/P level was significantly lower in group 2 compared to groups 1 and 3 ($p (U) = 0.03$). However, the Ca/P level was significantly lower ($p (U) = 0.01$). In groups 1 and 2, an increase in parathyroid hormone levels was noted in relation to group 3 and the control group ($p (U) = 0.01$), which causes a disruption in the processes of bone remodeling and mineralization, a decrease in bone density, and changes in bone architecture, and therefore increases the risk of fractures. Thus, the data obtained indicate that the problem of osteoporosis and osteopenia is relevant not only for women but also for young men suffering from epilepsy.

Clinical prognostic significance of seizures in the acute phase of aneurysmal subarachnoid hemorrhage

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Introduction

Seizures can be the first clinical manifestation of aneurysmal subarachnoid hemorrhage (aSAH), especially in the absence of the classic thunderclap headache. Symptomatic seizures occur in approximately 10% to 20% of patients with aSAH. The prevalence nearly doubles with continuous EEG monitoring due to detection of “silent” (nonconvulsive or purely electrical) seizures.

Methods

Data from 421 medical records of patients with aSAH were analyzed and divided into two groups: 1) with seizures at admission; 2) without seizures. Statistical analysis included the chi-square test, binomial and ordinal logistic regression.

Results

No statistically significant associations were found between cerebral aneurysm size or location and the occurrence of seizures (p=0.149, p=0.223, respectively). The presence of aSAH with a parenchymal component significantly increased the likelihood of seizures at admission (OR=2.828; CI=1.144–6.988; p=0.024). Patients with aSAH and both parenchymal and intraventricular components showed a tendency toward increased risk (OR=2.492; CI=0.934–6.646; p=0.068), while aSAH with an intraventricular component had no effect (OR=1.031; CI=0.381–2.790; p = 0.952). Patients with seizures were 2.6 times more likely to have higher WFNS grades (OR=2.60; CI=0.338–1.570; p=0.002). Seizures at admission tripled the risk of death (OR=3.032, CI=1.503–6.115, p=0.002).

Conclusions

Seizures at admission were associated with aSAH and parenchymal hemorrhage, higher WFNS severity, and increased mortality. Early seizures may serve as a marker of poor prognosis in aSAH.

Efficacy of temporal lobectomy in hippocampal sclerosis compared to medical therapy alone

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Relevance

Among structural forms of epilepsy, temporal epilepsy is the most common. Hippocampal sclerosis (HS) is the leading cause of temporal epilepsy. In cases of pharmacoresistant epilepsy, surgical treatment is highly effective. Additionally, a significant number of patients continue on medical therapy due to fear of surgery or other reasons.

Objective

To compare the effectiveness of medical and surgical treatment in patients with hippocampal sclerosis.

Materials

The study analyzed the disease course in 188 patients with confirmed hippocampal sclerosis who received treatment at the "Regional Center for Neurosurgery and Neurology" in Uzhhorod, Ukraine.

Results

Surgical treatment (temporal lobectomy) was performed on 69 patients with epilepsy due to HS.

One year after surgery, the following results were observed:

Engel Class I – 43 patients (62.3%)
Engel Class II – 21 patients (30.4%)
Engel Class III– 3 patients (4.3%)
Engel Class IV– 2 patients (2.9%)
Among patients who received only medical treatment, the outcomes were significantly less favorable:

Seizure-free – 4 patients (2.6%)
Auras only – 12 patients (7.8%)
Seizure frequency reduction 50% – 32 patients (20.9%)
No effect or 50% seizure reduction – 68.7% of patients
It should be noted that secondary generalized tonic-clonic seizures were controlled in most patients with HS, whereas complex partial seizures were more resistant to treatment.

Conclusions

Surgical treatment is significantly more effective than medical therapy for patients with HS. Importantly, treatment success was associated with the earliest possible initiation of both medical and surgical therapy. Patients with HS require timely and appropriate management, with early consideration of surgical treatment.

Pharmacological treatment after epilepsy surgery in children underwent SEEG.

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We retrospectively analyzed 100 pediatric patients with drug-resistant focal epilepsy (DRE) who underwent stereoelectroencephalography (SEEG) between 2012 and April 2024. Inclusion criteria were: a) age under 18 years; b) typical seizures recorded during SEEG monitoring; and c) at least 6 months of follow-up after surgery, including radiofrequency thermocoagulation (RF-THC). Seventy-eight patients met these criteria. The median age at SEEG was 10.7 ± 5.5 years [range: 4.5–15.3], and median epilepsy duration was 4.5 ± 4.2 years [range: 2.2–8.0].

Based on SEEG findings, 66 patients underwent surgery and/or RF-THC. Among them, 24 patients (36.4%) achieved Engel class Ia, 11 patients (16.7%) were classified as Engel Ib–d, and 31 patients (46.9%) in Engel II–IV. Antiseizure medications were successfully discontinued in only 16 patients (24.2%), of whom 14 were Engel Ia and 2 Engel Ib–d. The remaining 50 patients (75.8%) continued pharmacological treatment: among them, 9 were Engel Ia with ongoing drug tapering, and 6 were Engel Ib–d in whom medications were maintained due to either seizure recurrence after withdrawal or the complexity of the epileptogenic zone.

These findings underscore the need for studies aimed at guiding antiseizure drug tapering in Engel Ib–d patients, as well as pharmacological trials for those in whom surgery fails or proves only partially effective. A tailored pharmacological approach becomes crucial when surgery is not satisfactory or not fully satisfactory.

Changes in the use of cenobamate in refractory epilepsy in Norway

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Background: The new antiseizure medication (ASM) cenobamate (Ontozry) is approved as add-on treatment in adults from 18 years in refractory epilepsy since 2021 in Norway. The extent of use is not known so far.

Purpose: The aim of the present study was to investigate how the prescriptions and use of cenobamate changed and increased since its approval in Norway.

Methods: The Norwegian Prescription Database and Medicines Registry from the National institute of public health was used (2021-2024). This updated database now covers both prescriptions and use of drugs in hospitals and institutions, giving a total overview of drug use in Norway.

Results: The number of cenobamate users increased steadily from 37 users in 2022 to 447 in 2024. Women constituted a slight majority of users, 54-56%, from 2022 to 2024, respectively, while 51% of users were men in 2023. Highest numbers in 2024 were observed in the 25-29 age group (14%). Individuals 20 years accounted for a small proportion of users (4,5%); however, some off-label use in young patients was seen. No patients were below 10 years. The total defined daily doses (DDD) increased from 1,954 in 2022, to 92,168 in 2024. The annual increase in prescriptions suggests increasing confidence in cenobamate's clinical utility, despite its positioning as a later-line option. Details on the patient perspectives of use of new ASMs such as cenobamate will be further evaluated regarding efficacy, tolerability issues and adherence aspects in adult patients with epilepsy followed at Vestre Viken hospital.

Conclusion: The present results elucidate an increase in the use of cenobamate in Norway since its approval. The use of prescription data contributes to improved drug safety and drug surveillance as part of pharmacovigilance on a national scale.

Epilepsy and Digital Health: The Role of Wearables and Smartphone Apps

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Epilepsy management goes beyond seizure control. It requires long-term monitoring, strict adherence to medication, lifestyle adjustments, and active patient involvement. In recent years, advances in digital health have introduced new tools that empower patients and assist healthcare providers. Among these innovations, wearable devices and smartphone applications are gaining growing attention.

Mobile apps such as Seizure Tracker, EpiDiary, and Epilepsy Journal help patients and caregivers document seizure events, track medication intake, recognize potential triggers, and share data with medical professionals. These digital diaries offer structured and consistent reporting, which can improve clinical decision-making and help tailor treatment plans more accurately.

Meanwhile, wearable devices like Embrace2 and SmartWatch Inspyre are capable of detecting convulsive seizures and sending real-time alerts to family members or caregivers. Some devices also provide biometric data, such as heart rate and activity level, which may offer additional context before or after a seizure occurs.

These technologies are particularly valuable in outpatient care, where continuous EEG monitoring is not feasible, and during intervals between neurologist visits. They enhance communication between patients and clinicians, promote adherence, and offer a sense of safety and autonomy to individuals living with epilepsy.

However, their implementation remains limited in low- and middle-income countries, including parts of Central Asia, due to technological, economic, and infrastructural barriers.

This presentation will explore the current landscape of digital health tools in epilepsy care, their clinical potential, limitations, and strategies for implementation in resource-constrained settings to bridge the gap in epilepsy management.

Temporal Lobe Tumor-Associated Ictal Asystole in Infancy: A Case Report

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Ictal asystole is a rare but potentially life-threatening manifestation of focal epilepsy, particularly in infancy. When associated with structural brain lesions such as tumors, it presents significant diagnostic and management challenges. We report a rare case of ictal asystole secondary to a temporal lobe embryonal tumor in a 1-year-old child.

A previously healthy 12-month-old boy presented with recurrent episodes of unresponsiveness, perioral cyanosis, and altered muscle tone. Initial EEG and neurological assessments were inconclusive. Cardiac monitoring revealed sinus pauses exceeding 3 seconds, resulting in a diagnosis of sick sinus syndrome and pacemaker implantation. Postoperatively, persistent paroxysmal episodes with gaze fixation, asymmetric tonic posturing, and altered consciousness raised suspicion of seizures. Video EEG demonstrated interictal epileptiform discharges in the right temporal region. Brain CT revealed a large, contrast-enhancing mass in the right temporoparietal region with edema, midline shift, and obstructive hydrocephalus. Partial neurosurgical resection was performed. Histopathology confirmed an embryonal tumor with multilayered rosettes (WHO Grade 4). Postoperative recovery was favorable, with seizure control achieved following adjustment of anticonvulsant therapy. No acute focal neurological deficits were observed before or after treatment.

This case highlights the importance of considering neurological causes—including brain tumors—in infants presenting with syncope or suspected cardiac arrhythmias. Ictal asystole may mimic primary cardiac pathology but can result from focal seizures in tumor-affected regions. Early interdisciplinary evaluation is critical for accurate diagnosis and optimal management.

Unveiling viral meningitis in children and infants without cerebrospinal fluid pleocytosis

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Background: Aseptic meningitis is usually suspected in the presence of mild cerebrospinal fluid (CSF) pleocytosis. Nevertheless, viral meningitis without pleocytosis has been previously reported, yet CSF viral PCR testing is rarely performed when cell counts are normal. This study aimed to evaluate the diagnostic yield and clinical relevance of CSF viral PCR testing in children with suspected central nervous system (CNS) infection who present without pleocytosis.

Methods: A retrospective, single-center study was conducted between January 2021 and July 2023, including pediatric patients (0-18 years) who underwent lumbar puncture with CSF sample collection. Clinical, laboratory, and microbiological data were extracted. We specifically examined CSF viral PCR testing and its results in cases with normal CSF cell counts.

Results: Among 935 children, 76% had no CSF pleocytosis. CSF viral PCR was performed in 472 pleocytosis-negative cases, identifying viral pathogens in 31%. Enterovirus was the most common, especially in infants under 3 months, where 58% of enteroviral meningitis cases lacked pleocytosis. The negative predictive value (NPV) of pleocytosis for ruling out viral meningoencephalitis was 86.5% overall and 79% in febrile cases. Fever was significantly associated with positive PCR results, while bacterial infections were less frequent. Hospital stays were significantly shorter in pleocytosis-negative cases with a positive Enterovirus PCR compared to cases where PCR was not performed.

Conclusion: CSF viral PCR testing should be considered in infants, especially those under three months, presenting with suspected CNS infection without pleocytosis. Early viral identification may reduce unnecessary antibiotic use and hospitalization duration.

Factors Associated with Non-suicidal Self-Injury in Persons with Epilepsy: A Case-Control Study

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Introduction

Persons with epilepsy (PWE) are at increased risk for self-injurious behaviors, yet nonsuicidal self-injury (NSSI) remains under-investigated in this population. This study aimed to identify factors associated with NSSI among PWE.

Participants and methods

Thirty-six consecutively evaluated PWE with documented NSSI episodes in the past 12 months were identified at a general epileptic center. A control group of age- and sex-matched PWE without a history of NSSI was selected at a 1:3 ratio. All participants completed a case report form capturing demographic, clinical, and self-injury-related data. All participants filled out the brief Epilepsy Anxiety Survey Instrument (brEASI) and the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) to assess levels of anxiety and depression. Additional epileptological data were obtained from electronic health record system

Results

The final sample comprised 144 participants (53% female; mean age 25.3 ± 8.5 years), with 62.2% diagnosed with focal epilepsy. Compared to controls, NSSI in PWE was found to be associated with higher seizure frequency and were more likely to report depression, anxiety, lifetime suicidal ideation, lifetime suicide attempts, a history of psychiatric disorders, and medically documented alcohol abuse (all p 0.001). No significant differences were found between groups in other sociodemographic or clinical parameters.

Conclusion

NSSI in PWE is associated with a wide range of adverse psychological and clinical parameters, including those related to epilepsy, as well as suicidal behavior. Some of these factors are potentially modifiable, highlighting the need for NSSI screening in PWEs and the development of targeted interventions.

Single unprovoked and acute symptomatic seizures among adults in Moscow: etiology and mortality

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Background and Aims:

The generalized tonic-clonic seizure (GTCS) is the most common type of epileptic seizures presenting to emergency departments (ED). Differentiating between acute symptomatic seizures (ASE) and first unprovoked seizures (FUS) is crucial for prognosis and management. In this retrospective cohort study, we aimed to evaluate etiology and mortality in adults with ASE and FUS in Moscow.

Methods:

A total of 3190 consecutive cases of the first GTCS from the emergency ambulance database in Moscow were evaluated. The full information about these cases, including the history, previous and following hospitalizations, outcome of the index seizure, comorbidities, mortality, was collected from the Moscow «Unified medical information and analytical system data». ASE were defined according to Beghi E. et al. (2010). People with preexisting epilepsy (n=933), newly-diagnosed epilepsy (n=938) and other paroxysmal events (n= 38) were excluded. Chi-square test was used for group comparisons.

Results:

Out of 1281 adult patients with first-ever GTCS, 422 (32.9%) had ASE (mean age 46.0 [35.3-57.0], 76.3% males) and 859 (67.1%) had FUS (mean age 48.0 [36.0-61.0], 64% males). The etiology of ASE was alcohol withdrawal (73.4%), acute stroke (11.2%), traumatic brain injury (TBI, 3.5%). In patients with FUS, the etiology was unknown in 71.3%, 11.5 % had a history of stroke, 8.2 % had TBI, and 2.7% had tumors. The proportion of males was higher in ASE (p0.0001). Patients with FUS were older (p0.0001), but the one-year mortality (15.4% [95% ДИ 12.3-19.2] versus 11.7% [95% ДИ 9.8-14]) and three-year mortality (26.3% [95% CI 22.3-30.7] versus 24.4% [95% ДИ 21.8-27.3]) in patients with ASE were higher.

Conclusions:

Among patients with the first-ever GTCS, the proportion of FUS was higher than ASE. The etiology of ASE was mostly alcohol withdrawal. The one-year and the three-year mortality were higher in patients with ASE compared to patients with FUS.

Stimulation-induced hippocampal seizures and cardiovascular instability

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Background

Seizures involving hippocampus are known to cause heart rate instability, but the influence of hippocampal seizures on blood pressure regulation remains unclear. In this study we aimed to evaluate how stimulation-induced hippocampal seizures affect the regulation of blood pressure in patients with drug resistant epilepsy undergoing presurgical evaluation.

Material and methods

In patients undergoing stereo-EEG (SEEG) monitoring with electrical stimulation (ES), we recorded heart rate as electrocardiographic RR-intervals and beat-to-beat blood pressure (BP) during ES-induced seizures. We compared values of arterial baroreflex sensitivity (BRS), systolic (SBP) and diastolic BP (DBP), and coefficient of BP variability (CV) before and after hippocampal seizures. Statistical analysis was performed using the Wilcoxon test (p 0.05).

Results

In 35 patients (median age with interquartile range 30 years [25-39 years], 22 women), 52 hippocampal seizures (right, n=28, left, n=24) were analyzed. Right hippocampal seizures increased SBP (p=0.004), DBP (p0.0001) levels and CV values (p0.0001), while left-sided seizures decreased SBP (p=0.04) and DBP (p=0.02) levels, but elevated CV values (p0.0001). BRS decreased only in right-sided seizures (p=0.001).

Conclusion

Hippocampal seizures induce lateralized BP dysregulation, with right-sided seizures causing pressor effects and baroreflex suppression, while left-sided seizures lead to depressor responses. These findings highlight the hippocampus's role in ictal cardiovascular instability, potentially implicating autonomic dysfunction in SUDEP risk.

Oxcarbazepine Therapeutic Drug Monitoring During Pregnancy

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Background: Oxcarbazepine (OXC) is a commonly used anti-seizure medication (ASM) effective primarily against focal onset seizures. OXC is sometimes prescribed to women of childbearing age and occasionally during pregnancy. Physiological changes throughout gestation may alter the pharmacokinetics of OXC, impacting serum levels and therapeutic efficacy. The goal of our study is to evaluate the impact of pregnancy on OXC metabolite serum concentrations and support clinical decision-making regarding dose adjustments during and after pregnancy.

Methods: This retrospective, observational study included five women with epilepsy treated with OXC, followed at the epilepsy in pregnancy clinic in Tel Aviv Sourasky medical center (TASMC). Since OXC is a prodrug of licarbazepine (LIC or 10-OH-carbazepine) that is OXC active entity in humans. Trough (Cmin,ss) LIC serum levels were collected during pregnancy and either before conception or postpartum. At each measurement, the corresponding dose and gestational week were documented. Monitoring of LIC Cmin,ss levels were done using tandem mass spectrometry (MS/MS) that was performed at a single lab in TASMC. Descriptive statistical analysis was conducted to compare serum levels between pregnant and non-pregnant states, with dosing recorded for context.

Results: A total of 28 measurements were analysed, with a mean LIC Cmin,ss serum concentration during pregnancy of 12.7 µg/mL, compared to 18.1 µg/mL outside of pregnancy. LIC Cmin,ss serum levels during pregnancy were significantly lower compared to levels measured outside of pregnancy, suggesting an increased LIC clearance or altered pharmacokinetics during gestation. This suggests increased drug clearance or altered absorption during gestation. In contrast, higher LIC Cmin,ss levels were observed postpartum or pre-conception even at lower or equivalent doses.

Conclusions: The serum levels of OXC active entity LIC decline during pregnancy despite therapeutic dosing, highlighting the importance of routine drug monitoring and individualized dose adjustments. These findings support the implementation of proactive LIC serum monitoring protocols and dose optimization strategies for women treated with OXC during pregnancy and the postpartum period.

Cenobamate use in people with drug-resistant epilepsy and learning disability: a case series

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Objective: Cenobamate is a new anti-seizure medication for people with drug-resistant focal epilepsy with proven efficacy in clinical trials, particularly for generalised tonic-clonic seizures. Data on its effectiveness and tolerability in people with drug-resistant epilepsy and learning disability are scarce. To identify further individuals who may benefit from cenobamate therapy, we report eight cases in which the initiation of cenobamate resulted in a favourable outcome.

Methods: Review of a cohort of adults with severe drug-resistant epilepsy and learning disability, living at the Chalfont Centre for Epilepsy, whose seizure frequency decreased and/or cognition and behaviour improved after the initiation of cenobamate.

Results: Eight individuals (four females; median age 37 years, range 23–60 years) who experienced a reduction in seizure frequency along with improvements in cognition and behaviour after starting cenobamate are reported.

Significance: Cenobamate is potentially effective in people with drug-resistant epilepsy and learning disability by reducing seizure frequency and improving cognition and behaviour. The rate of titration and maximum dose should be determined on an individual basis.

Enantioselective Comparative Analysis Of The Anticonvulsant Potency Of Fenfluramine And Norfenfluramine In Mice

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Abstract

Objective

The in vivo effects of fenfluramine result from the combined actions of four active molecular entities (*l*-fenfluramine, *d*-fenfluramine, and the corresponding enantiomers of the primary metabolite norfenfluramine). Each of these compounds has different properties, with cardiovascular toxicity risk being ascribed primarily to the *d*-enantiomers. To determine whether *l*-fenfluramine or *l*-norfenfluramine is a better candidate for development as an enantiomerically pure antiseizure medication, we investigated dose–response and brain/plasma concentration–response relationships for each of the four individual enantiomers in mice.

Methods

Antiseizure activity was evaluated in the maximal electroshock (MES) model at the time of peak effect. Neurotoxicity was assessed by determining minimal motor impairment (MMI) in the rotarod test. Median effective dose (ED_{50}), median toxic dose (TD_{50}), median effective concentration (EC_{50}), and median toxic concentration (TC_{50}) in plasma and brain were estimated from dose– and concentration–response curves after administration of each individual enantiomer. Protective indexes (PIs) were estimated based on dose (TD_{50}/ED_{50}) and plasma/brain concentrations (TC_{50}/EC_{50}).

Results

The four enantiomers differed in antiseizure potency and neurotoxic activity. *d*-Norfenfluramine had the highest potency, but it also had the highest toxicity and the lowest PI. Differences in antiseizure potency and toxicity estimated from plasma and brain concentrations were more prominent than those estimated based on dose. *l*-Fenfluramine had greater potency than *d*-fenfluramine and *l*-norfenfluramine, and was overall the compound with the highest PI (6.3 based on dose, 41.6 based on plasma concentrations, and 39.2 based on brain concentrations).

Significance

These findings are relevant in determining which enantiomer is most suitable for clinical development as a stereoselectively pure follow-up compound to the marketed racemic fenfluramine, and indicate that *l*-fenfluramine has superior antiseizure activity over *l*-norfenfluramine in the MES model. This study also illustrates the limitations of relying solely on dose–response curves, and the added value of assessing concentration–response relationships.

α-Fluorine Substitution in Medium-Chain Fatty Acids to Enhance Anti-Epileptic Activity

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Background:
Epilepsy remains a major neurological disorder, with current treatments such as valproic acid (VPA) limited by toxicity and incomplete seizure control. Medium-chain fatty acids (MCFAs), structurally related to VPA and linked to the ketogenic diet, offer a promising scaffold for developing safer anti-seizure agents. Chemical modification by α-fluorine substitution may enhance pharmacokinetic stability, brain penetration, and therapeutic efficacy.
Methods:
A library of α-fluorinated MCFAs was synthesized and verified for purity by NMR and HPLC. Neuroprotective potential was evaluated in SH-SY5Y neuroblastoma cells and primary cortical neurons using MTT viability assays and live-cell calcium imaging under seizure-like conditions induced by picrotoxin and 4-aminopyridine. *In vivo* efficacy was assessed in a Pentylenetetrazol (PTZ)-induced seizure mouse model, measuring latency, severity, and mortality.
Results:
Among the tested compounds, 2-fluorodecanoic acid (2-FD), 2-fluorooctanoic acid (2-FO), and 2,2-difluorodecanoic acid (di-F) demonstrated low cytotoxicity. All fluorinated derivatives reduced seizure-like calcium oscillations *in vitro*, with di-F showing the strongest suppression of frequency and amplitude. *In vivo*, di-F pretreatment significantly reduced seizure incidence and severity while increasing latency to onset, outperforming both VPA and monofluorinated analogs.
Conclusion:
α-Fluorination of medium-chain fatty acids enhances anti-seizure efficacy and tolerability. The difluorinated compound di-F exhibited the most potent protective effect, supporting α-fluorine modification as a rational strategy for developing next-generation anti-epileptic drugs.